THE VENEREAL DISEASES

A Manual for Practitioners and Students

BY

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TO

THE LATE CHARLES GIBBS, F.R.C.S.

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PREFACE TO SECOND EDITION

The important change in this edition is the addition throughout the book of treatment methods using penicillin. Penicillin is not yet universally available, so I have thought it best to add this information rather than to rewrite the existing chapters on treatment also there are times when penicillin therapy can be incorporated into the older schemes of treatment. An outline of the applications and instructions for administration of penicillin (as known at present) will be found in the Introduction.

The sections on non-gonococcal urethritis have been re-written and expanded and a note on Reiter's syndrome added. Massive arsenotherapy has also been brought up to date although interest in this subject is naturally less since the advent of penicillin.

Many small amendments have been made in the text where they have been indicated by changes in practice, and I am grateful to reviewers and friends who pointed out errors and omissions (minor I am glad to say) in the first edition.

I must again acknowledge my indebtedness to my wife and to Mr L. J. P. Brimble for their help in preparing this new edition.

JAMES MARSHALL

PREFACE TO FIRST EDITION

The importance of venereal diseases and the rapid progress in research on them, together with changes in treatment, call for a general review of the diagnosis and treatment of venereal diseases

This book has been written, therefore, to satisfy this need and since it is intended especially for practitioners and students (not for research venereologists) special care has been taken to keep the practical problems to the fore.

A subject of this practical nature needs careful illustration

and a special point has been made of this Most of the illustrations are original and have recently been photographed from actual cases for use in this book.

I am particularly grateful to Major Sydney Laird R.A.M C., who has read the manuscript, pointed out errors and omissions and made the most pertinent criticisms

My wife has been of inestimable help in typing the manuscript and reading the proofs.

Mr L. J F Brimble, who has edited this book has given me invaluable assistance in preparing manuscript and illustrations and in reading the proofs.

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The bulk of the clinical photographs have been taken specially for this book by Mr Norman K. Harrison, of the Topical Press Agency Ltd. Other illustrations were supplied by the Wellcome Foundation (these were re-photographed for this book by Mr A. Michiell) (Figs. 1 11 21 29, 51 54, 56 58, 61 63 64, 68, 69, 70, 71 73 75 79, 81 83 84) Messrs. Parke, Davis & Co (some of the coloured plates Nos. I II III IV V VI (right)) Dr Sydney Thomson (Figs. 38 41 52 53 57 59, 60, 67 78 89) and Messrs. Cassell & Co Ltd. (photograph formerly published in Malcolm Morris's *Diseases of the Skin*, 5th Edition) (Fig 40) and Professor J H Dible and Dr J McMichael and the Editor of the *British Journal of Venereal Diseases* (four photomicrographs in the issue of the *Journal* for September 1943) (Figs. 61 A–D)

All the line drawings have been prepared from originals specially drawn by Dr C. V Spark.

I am indebted to all these authorities for their considerable help with the illustrations.

COLOUR PLATES

retrospect, considering the virtual impossibility of giving adequate arsenical treatment to men in the invading armies, the results were reasonably good Relapses after penicillin treatment, as after any rapid method tend to occur within a few months of treatment (late relapses have yet to be properly assessed) and re treatment by vigorous methods can usually remedy the situation.

Progress was, until recently hindered by the necessity of conserving penicillin and the dosage used has tended to be the minimum likely to cure. The best results in syphilis have, so far been obtained when penicillin and arsenicals (and some times bismuth) have been used simultaneously and a risk of arsenical toxic effects still persists When all the possibilities of penicillin, in higher dosage, over longer periods by divided courses, with other remedies and with fever etc. have been fully investigated there will doubtless be found some method of treating syphilis less hazardous than those of the past. The time necessary for treatment will certainly be reduced but Ehrlich s hope of *magna therapia sterilisans* is still as far away as ever

Penicillin s place in the treatment of gonorrhoea is already established. Its use in the armies in 1944 was most opportune, for not only did it reduce time lost to a minimum but also it solved the difficulty of dealing with the increasing numbers of sulphonamide resistant cases which in certain areas presented an alarming problem.

A major problem in the penicillin treatment of the venereal diseases in civil life has been the necessity for frequently repeated injections. This meant hospitalization in all cases where it was used for syphilis, and even in some cases of gonorrhoea. Penicillin is inefficient and not uniform in effect when given by the oral route as doses must be at least five times as great as those necessary to achieve the same results when injected

The use of retarding substances (oil-beeswax) in which penicillin can be suspended has made the ambulant treatment of syphilis possible by reducing the number of doses necessary to maintain effective blood-levels to one or two each day I am, personally dubious of this method and prefer whenever possible to hospitalize patients so that they may have peni cillin in aqueous solution by frequently repeated injections.

A point still undecided is whether repeated high peaks of blood concentration of penicillin as obtained by injections of aqueous solution are more effective than the longer maintained lower levels produced by oil wax suspensions.

In using penicillin the important point to remember is that it is virtually non toxic and therefore, that over treatment should be the order of the day

The practitioner who contemplates treating venereal diseases will be well advised to keep abreast of the frequent changes in penicillin therapy by consulting the journals and keeping in touch with the director of the local venereal diseases clinic.

PREPARATION AND ADMINISTRATION OF PENICILLIN

Injections of penicillin in solution or in oil-wax suspension must be made with full aseptic technique. Syringes and needles must be sterilized by boiling or by autoclaving before each injection and must be assembled without contamination. Sterilization by immersion in spirit is not permissible. Spirit may be used to clean the skin at the site of injection, but it should be allowed to dry before the needle is inserted.

Aqueous solutions should be made up with sterile distilled water Nothing is gained by using saline solution as the solvent. The use of Novocaine to decrease local pain at the site of injection is not, in my experience, worth while.

Penicillin for the making of aqueous solutions is a light brown or yellow powder supplied in rubber-capped vials containing (usually) 100 000 units. Distilled water is injected through the cap and solution rapidly takes place. The amount of water used for each vial will vary with the dosage selected, but it is not necessary to use more than 1-2 c.c. of solvent for each dose. To avoid loss, when extracting the last dose, the cap should be ripped off and the needle inserted into the vial. Penicillin in solution should be kept cool in a refrigerator if possible, and used within 48 hours of preparation.

Intramuscular injections are made in the usual way into the upper and outer quadrant of the buttock, using the sides alternately Personal experience with a vast number of patients has shown that, even with the many injections necessary in syphilis, it is seldom necessary to use other sites. If a patient

should complain of severe local pain the muscles of the outer sides of the thighs can also be used, but this site is apt to become even more tender than the buttocks. Local pain is caused by certain batches of penicillin no doubt because of some impurity and in general the darker the shade of the penicillin powder the more likely is it to give this trouble.

Oil-wax suspension of penicillin (Injectio Penicillum Oleosa B P) contains 125,000 (or more) units per c c. of an arachis oil beeswax (or ethyl oleate beeswax) mixture. It should be stored in a refrigerator if possible, but will retain its potency at room temperature for six months. Th oil is rather thick and in cold weather the vial (which contains 10 c.c.) must be warmed a little before it can be extracted Extraction is facilitated by using a wide bore needle and a perfectly dry warmed syringe. A smaller needle is exchanged before making the injection Alternate buttocks are used for the injections, which may sometimes cause considerable local pain This can be minimized by prolonged deep massage after injection Local induration sometimes occurs, but has always subsided in my experience, after local heat without abscess formation

PART I

GONORRHOEA

Chapter I

INTRODUCTION

Gonorrhoea is a contagious disease usually affecting the genito-urinary tract in both sexes but capable of widespread dissemination throughout the body General effects due to absorption of toxins through undrained local foci of infection are fairly common but bacteriaemia and pyaemia are very rare.

The infection is contracted by the adult during sexual intercourse in the vast majority of cases but female children are most commonly infected by contact with articles contaminated by a person suffering from the disease. Extra genital infections of the eye are seen in adults as a result of auto-infection or of contact with infected articles. In infants eye infections are contracted during the birth process. The rectum is sometimes infected in male homosexuals and proctitis in the female is not uncommon the infection being spread directly by vaginal discharge. The gonococcus has also but rarely been the cause of a stomatitis, and has been found in cutaneous ulcers.

The incubation period is generally from 36 hours to 8 days, but the broadest limits given by various authors are 12 hours and 28 days.

The chances of infection by intercourse with an infected person are very much higher for the female than for the male, mainly for anatomical reasons. Cases are most dangerous during the acute stage. Gonorrhoea in the male is usually contracted from young women of the amateur class, the professional prostitute only providing a comparatively small number There are a number of reasons for this. First, amateurs greatly outnumber professionals secondly the professional is very much more likely to adopt prophylactic

measures so that her livelihood cannot be endangered thirdly the older professional has usually been well vaccinated by many attacks of gonorrhoea in the past and is unlikely to derive any satisfaction from the act of coitus and so wash out her gonococci in gland secretions during an orgasm

Women with a chronic infection are most likely to be dangerous just before and just after a menstrual period when the cervical and other glands are secreting most and washing out any gonococci they may contain

Gonorrhoea can be transmitted by a man or woman during the incubation period before any signs or symptoms appear and a very large number of marital infections occur for this reason In any event where a person has so unwittingly exposed his or her partner to infection the doctor should insist upon the suspect being kept under observation for a time sufficient to cover the longest incubation period Simple measures can provide adequate prophylactic protection against gonorrhoea and this subject will be discussed further in the treatment of the disease

Dr Jules Janet in his text book *Diagnostic et traitement de la blennorragie* gives this simple prescription for any man wishing to contract a gonorrhoea Pick any woman at all *no matter how* seldom she may have strayed who has just finished a menstrual period and sacrifice to Venus with her in a place where it is impossible for her previously and for you afterwards to do the ritual ablutions If in these circumstances, you do not catch the gonorrhoea it is because you have a special god protecting you.

Gonorrhoea, unlike syphilis has always been known in the Old World The name is of Greek origin and means literally a flow of semen References in the Old Testament to an issue probably describe gonorrhoea

BACTERIOLOGY OF GONORRHOEA

The gonococcus is a Gram-negative diplococcus The cocci are kidney-shaped and arranged in pairs the concave margins of the two cocci facing each other In size each coccus is 0·8 μ long by about 0·6 μ broad They are non motile and non-capsulated, but the appearance of capsulation is sometimes given in stained specimens by a ring of

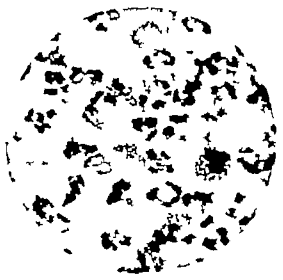


Fig —GONOCOCCI IN A SMEAR OF PUS

fainter staining round certain pairs. The gonococcus, in preparations of pus, is seen lying within the pus cells (Fig 1)

Extracellular diplococci are also found between the cells or lying on epithelial cells The finding of extracellular Gram-negative diplococci alone in a preparation is not sufficient evidence for a diagnosis of gonorrhoea. If the diplococci are indeed gonococci, a careful search should reveal intracellular forms. In acute cases there should be no difficulty in making a diagnosis from stained smear preparations but in chronic cases it is sometimes more difficult to find the gonococcus, and cultural methods are found more successful, particularly in women.

In court of law it is advisable to be able to produce positive cultural evidence to substantiate a diagnosis made by smear examination

Apart from the common sites of the urethra in the male, the urethra and cervix in the female, the gonococcus can be isolated locally in cases of epididymitis, prostatitis, proctitis, salpingitis, cystitis, pyelonephritis and peritonitis On rare occasions it is found in cases of arthritis and tenosynovitis Gonococcal bacteriaemia or pyaemia is also possible. Proved

cases of gonococcal stomatitis and cutaneous infection are also described.

Cultural Methods

The gonococcus grows fairly well on culture. It is generally agreed that the best medium is a nutrient agar containing 10 per cent of hydrocele fluid at pH 7·5. Other successful media are the egg albumen medium of Price and the Nile Blue medium of Gardner. Growth in serum broth is very poor and in stab cultures nil.

In culture, after twenty four hours, the colonies are round domed or umbilicated translucent and greyish white in colour. The colonies are 0·5–1 mm in diameter sharp-edged with a smooth glistening surface. Later they may increase in size and become rough. In order quickly to distinguish colonies of gonococci in a mixed culture, a 1 per cent solution of dimethyl paraphenylene diamine hydrochloride in distilled water is poured over the medium. Colonies of gonococci are stained a faint pink colour which in time darkens and becomes black.

Suspect colonies are picked off and examined microscopically to confirm. In inoculating cultures with suspect material the material should be well rubbed on for about one minute. The best results will be obtained by inoculating the medium as soon as the material is obtained from the patient the medium being immediately returned to the incubator.

The practice of taking swabs to be sent to a laboratory for subsequent inoculation on to the medium is not likely to yield a high percentage of positive results. The taking of specimens in glass capillary tubes for transmission to a laboratory offers a more hopeful solution in those cases where direct inoculation of medium is not possible.

The Complement Fixation Test

This is a serum test of the Bordet Gengou variety. It is a test for the presence of gonococcal antibodies in the serum not for the presence of gonococci in the body. It resembles the Wassermann reaction (see p 123) except that a true antigen prepared from gonococci is used.

The technique of the test varies in the hands of different pathologists but a high degree of accuracy has been attained

in some cases. The antigen generally employed is prepared by dissolving gonococci — one or many strains may be used — in sodium hydroxide, adding hydrochloric acid and dissolving the precipitate in more sodium hydroxide.

According to I N O Price, in untreated cases a positive result is found in the first week in 27 per cent, in the second week in 46 per cent, in the third week in 70 per cent, in the fourth week in 89 per cent, and in the fifth and subsequent weeks in 100 per cent of cases. These results are closely paralleled in the findings of the London Lock Hospital Research Unit

A positive test can be produced experimentally by the injection of vaccine Positive results are found in arthritis, prostatitis, vesiculitis, salpingitis and, in fact in any condition where gonococci are pent up without free drainage so that absorption of toxin is possible. A negative reaction is to be expected in early cases and where there is free drainage. As in syphilis, a certain time is required for the body to elaborate antibody in sufficient quantity to be demonstrable by the test Experimental positive complement fixation tests become negative after six to eight weeks

Opinions differ as to the significance of a persistent positive complement fixation test for gonorrhoea in the absence of any other clinical or pathological signs, but a strongly positive result given by a good pathologist in such a case is an indication for further exhaustive investigation. No test of cure is reliable without this test The number of positive tests returned has declined markedly since the advent of the sulphonamides. In a well handled early gonorrhoea the test is now seldom positive, as the infection is eradicated before there is time for demonstrable antibody to be produced.

In practice there is no indication for the performance of the complement fixation test in straightforward cases until the test of cure is reached. The complement fixation test is a valuable aid to diagnosis in the investigation of rheumatism of unknown origin, in iritis and in gynaecological conditions where salpingitis may be suspected

In chronic or complicated gonorrhoea under treatment, reversal of a positive complement fixation test to negative is evidence of the establishment of drainage and of successful treatment. One has sometimes been confronted with cases of

severe complicated gonorrhoea in which the complement fixation test is persistently negative Such cases are explained by the pathologist as lacking in resistance and unable to form antibodies against the gonococcus

From the foregoing description it will be gathered that the complement fixation test even when done by the best pathologists, is not to be regarded as giving the final word in gonorrhoea It must always be used as a guide only and results interpreted in conjunction with other pathological and clinical findings

Chapter II

GONORRHOEA IN THE MALE

UNCOMPLICATED AND RESISTANT CASES

The original site of infection is the urethra in the vast majority of cases. If early treatment is instituted, the disease will spread no further Local spread is not uncommon in untreated or badly treated cases prostatitis and epididymitis being the most frequent complications. Metastatic complications are less common than local complications and usually occur later in the course of the disease.

Signs and symptoms of acute gonorrhoea are usually obvious enough to bring the male under treatment very quickly Sometimes the urethritis is very mild and transitory and the patient may present himself with some complication such as epididymitis and giving no history of urethral discharge.

Diagnosis of acute gonorrhoea in the male is simply and quickly made by finding the gonococcus in a smear of urethral pus, but in chronic cases much more difficulty is experienced Tests must be more searching and cultural and serological examinations are often necessary

ANATOMY

The Urethra

The male urethra extends from the neck of the bladder to the tip of the penis ending at the meatus (Fig 2) It is 6-8 inches in length and is divided into three parts. The proximal 1¼ inches, the prostatic urethra, passes through the prostate gland. Its cross section is horseshoe-shaped with the convexity forwards. The verumontanum projects as a ridge from the posterior wall with a depression the prostatic sinus into which open the prostatic ducts, on either side The ejaculatory ducts open upon the edges of the sinus pocularis, a depression on the verumontanum *(Fig 3)*

The membranous part of the urethra extends from the prostate to the bulb is ¾ inch in length, and is contained between the layers of the triangular ligament. The compressor urethrae muscle surrounds it.

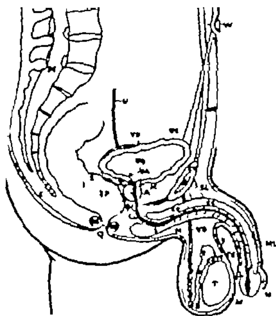


Fig 2.—General Anatomy of the Male Genito-urinary System

A, prostatic gland; *B* compressor urethrae *C*, Cowper's gland; *CC*, corpus cavernosum *CS*, corpus spongiosum *D* bulb *E*, epididymis *E1* globus minor *E2* globus major *EC*, tip of coccyx *F* Littré follicles *G* glans penis; *H* bulbous urethra *K* internal sphincter *L*, lacuna magna; *L1* 5th lumbar vertebra *M* meatus of urethra *ML*, lacunae of Morgagni *MR*, rectus muscle *N* fossa navicularis; *P* triangular ligament *Q* anus *R*, rectum *RS*, rectal sphincter *S* seminal vesicle *SC*, spinal canal *SL*, suspensory ligament *SP* sinus pocularis *S1* 1st sacral vertebra *ST* symphysis pubis *T* testicle *TG* Tyson gland and duct *U* ureter *UA* orifice of ureter *UB* urinary bladder *UC* urachus *VD* vas deferens *VE* vasa efferentia *W* umbilicus *XX* anterior urethra *XJ* membranous portion of posterior urethra *J-J* prostatic portion of posterior urethra

The penile urethra passes forward in the substance of the corpus spongiosum and is 4–6 inches in length The ducts of Cowper's glands open into the floor of the penile urethra in the bulb Just behind the meatus an enlargement of the urethra is known as the fossa navicularis The glands of Littré open into the floor of the penile urethra.

In the roof and sides of the anterior urethra are numerous small depressions, the lacunae of Morgagni the largest of which the lacuna magna is just behind the fossa navicularis.

The urethra is covered by a mucous membrane of stratified epithelium in the fossa navicularis of columnar epithelium in other areas and in the gland ducts Under the mucous membrane is submu us tissue containing longitudin l plain muscle fibres

The Prostate Gland

The prostate gl.
is rou hly py

posterior surface lies against the rectum and its anterior below the symphysis pubis On either side are the levatores ani. The ejaculatory ducts perforate the gland to open into the prostatic urethra The whole gland is surrounded by a fibrous fascial sheath. The glandular tissue is embedded in plain muscle and connective tissue. The glands open through their ducts into the prostatic urethra on either side of the verumontanum.

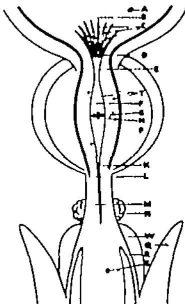


Fig 3.—The Posterior Urethra in Lateral Section

A, ureteric orifice; *B* trigone of bladder; *C*, frenum of verumontanum *D* prostatic fossette; *E*, crest of verumontanum *F* verumontanum; *G*, orifice of left ejaculatory duct; *H* sinus pocularis *K* urethral crest *L-M* membranous urethra; *N* Cowper gland; *P* prostate gland; *Q*, crus penis; *R*, corpus spongiosum; *S*, orifice of Cowper's gland duct; *T* openings of prostatic glands; *W* left side of bulb

The Seminal Vesicles Vasa Deferentia, and Epididymes

The seminal vesicles are pyramidal sacculated pouches lying between the bladder and the rectum and above the prostate gland. Each duct joins the corresponding vas deferens to form the common ejaculatory ducts (Fig 4)

The vas deferens leads from the epididymis to join the duct of the seminal vesicle and open into the urethra. It passes through the inguinal canal and along the side of the bladder and is lined by a columnar epithelium.

The epididymis consists of an upper globus major a body and a lower globus minor which lies behind the testicle to which it is attached by the vasa efferentia. Its structure is of a convoluted tubule lined by columnar ciliated epithelium.

Cowper's Glands

The two Cowper's glands lie on either side of and behind the membranous urethra between the two layers of the triangular ligament They are about the size of a pea and their ducts pass forward to pierce the anterior layer of the triangular

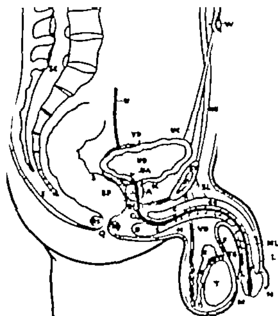


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The Prostate Gland

The prostate gland surrounds the neck of the bladder and is roughly pyramidal in shape with the apex downwards Its

posterior surface lies against the rectum and its anterior below the symphysis pubis. On either side are the levatores ani. The ejaculatory ducts perforate the gland to open into the prostatic urethra. The whole gland is surrounded by a fibrous fascial sheath. The glandular tissue is embedded in plain muscle and connective tissue. The glands open through their ducts into the prostatic urethra on either side of the verumontanum.

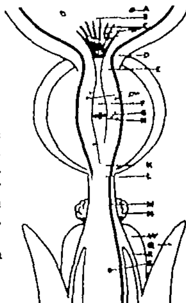


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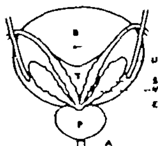


Fig 4.—POSTERIOR ASPECT OF THE PROSTATE GLAND AND SEMINAL VESICLES

A urethra; *B* bladder; *E*, ejaculatory ducts *P* prostat gland *S* seminal vesicle; *T* external trigone *U* ureter *V* vas deferens

ligament and open into the most proximal part of the penile urethra

EXAMINATION OF PATIENT

A full history should be taken including an account of the present attack, all recent exposures to infection marital or otherwise, and details of any previous venereal or genito-urinary infection with dates and treatment

It is best to examine the patient stripped or at least with the shirt held up to the chin and trousers down to the ankles Being satisfied that there is no evidence of syphilis or skin disease by inspection of skin mouth and anal region a detailed examination of the genitals is made. With prepuce retracted the glans is cleansed if necessary with a swab soaked in saline and any sores or balanitis are noted The groins are palpated for enlarged lymph glands and the spermatic cords and epididymes are felt

If no urethral discharge is visible gently draw a finger along the under surface of the urethra and massage the urethral contents to the meatus. A smear can now be made by introducing a sterile platinum loop into the urethra for a short distance, the lips of the meatus being held open (Fig 5) The loop must not scrape or injure the urethral wall

A thin film is made of the discharge on a glass slide and the loop is sterilized immediately afterwards in a flame If the pus is very thick it is permissible to thin it upon the slide with a drop of saline so that the smear shall not be too thick for easy examination

The appearance of the meatus is noted and a search is made for any infected para urethral ducts The patient should now urinate into two conical glasses a few inches into the first glass the rest into the second The appearance of the urine and of any debris threads blood or clots in it are noted Acetic acid should be added to any cloudy urine to avoid confusion by phosphates Urines will be classified into cloudy for the most turbid specimens hazy or clear Individual

practitioners will no doubt invent some classification or variation on the above system to assist them in watching the progress of their cases by examination of the urine.

In an early acute case rectal examination on the first visit is unnecessary unless the symptoms suggest some acute process in the prostate gland Even then, examination of the prostate and vesicles must be conducted with extreme gentleness to avoid spread of infection In the acute case a smear is now stained and examined and the patient is given the appropriate treatment and instructions If the case is not one of acute infection, the examination will be more exhaustive and will include tests on the lines described under the heading of Tests for Cure (p 49)



Fig. 5.—Taking a Specimen of Pus from the Urethra

ACUTE URETHRITIS

The first sign of urethritis is generally the appearance of a purulent or muco-purulent discharge, white or yellow in colour and sometimes blood-stained The lips of the meatus are red swollen and pouting There is also in most cases some frequency of urination and dysuria, which symptoms may precede by some hours or days the appearance of the discharge. There may be some general *malaise and even* slight fever Painful nocturnal erections are common

The character of the discharge varies according to the incubation period and in general one can say that it is frankly purulent when the incubation period is short and is inclined to be muco-purulent when the incubation period is more than a week.

Diagnosis is made by finding the gonococcus in a smear of the pus taken from the urethra and stained by Gram's method (see p 13 for technique) The use of a single stain such as methylene blue in diagnosis is to be deprecated In doubtful cases when possible, a culture of the pus is indicated and in certain cases for example marital infection where an accurate diagnosis is essential it may be found to be politic to delay a little the start of treatment until several smears have been examined if an exact diagnosis cannot be made at once

An accurate diagnosis is usually difficult and often impossible after medication with a sulphonamide, and chemotherapy before diagnosis is most unfair to both patient and consultant Only when a doctor has no diagnostic facilities at hand it may be necessary to take a smear send it to a pathologist and start treatment on the clinical diagnosis before a result is returned so that the disease may not be aggravated by delay

In examining the penis and discharge no vigorous massage or squeezing is to be used to express the pus This unfortunate habit common to patients and doctors, is dangerous and may cause spread of infection into deeper tissues

The urine in acute gonorrhoea is cloudy or hazy with pus and debris and may possibly be blood-stained At the first examination after taking the smear the patient is instructed to retract the prepuce cleanse the end of the penis and urinate into two glasses about four inches in the first glass the rest in the second This avoids contamination of the urine by subpreputial discharges The two-glass test is reputed to show whether the infection lies in the anterior urethra or in both anterior and posterior

In the past it has been the custom arbitrarily and clinically to divide the urethra into an anterior and a posterior part, the anterior urethra extending from the meatus to the anterior layer of the triangular ligament, the posterior comprising the membranous and prostatic urethrae

According to Janet the posterior urethra drains into the bladder and the anterior into the shirt The first glass therefore should contain the washings of both parts of the urethra while the second passed over an anterior urethra washed clean by the first specimen should indicate the state of the posterior urethra Both glasses cloudy would indicate an infection of

the whole urethra, while a clear second glass would mean that the anterior urethra only was affected.

This is very probably not the case, for how are we to tell that the first jet of urine has indeed washed the anterior urethra quite clean? Although the two-glass test is not an accurate guide to the anatomical site of the disease, it is an indication of the severity of the infection and amount of pus formation In the patient who reports at the first sign of discharge, the second glass is usually clear but in the later case both glasses may be cloudy and the patient should be watched more carefully

The gonococcus is no respecter of anatomical boundaries, and it is difficult to see any reason for continuing to talk of anterior and posterior urethritis as separate clinical entities. It is probable that in gonorrhoea the infection is of the whole urethra, although in the early stages of the disease, the signs may be most evident in the anterior part of the canal, but in later stages infection in the prostatic urethra and adjacent organs is likely to assume greater importance. It is therefore better to visualize gonorrhoea as pan urethritis with local incidents at different stages rather than as a disease liable to confinement by arbitrary anatomical boundaries

TREATMENT OF ACUTE UNCOMPLICATED GONORRHOEA

Whenever possible the patient should be confined to bed for at least the first forty-eight hours, and preferably until chemotherapy has ceased. A bed patient has a much better chance of speedy recovery of avoiding complications and toxic effects of chemotherapy than one who continues to work during treatment

It is well to start with an empty bowel and an enema or purgative on the first day may save the patient much discomfort from minor toxic effects of treatment. Diet should be light but its composition can be left to the patient For the first forty-eight hours a fluid diet is best. There is no need to withhold foods containing sulphur from patients taking sulphonamides. This was previously considered important, but experience has shown that diet has but little effect on the incidence of toxic effects.

Fluid intake is very important in the avoidance of renal toxic effects. A minimum of six pints of fluid a day is essential.

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Patients should be instructed to drink a pint of fluid each time they take tablets and as much as possible between times. Any bland fluid can be used but alcohol is strictly forbidden. When patients are instructed on this point, all the various kinds of alcoholic beverages must be specified for many people only associate spirits with the word alcohol

Patients should be told to watch the urine and report any abnormality either in quantity or in quality Any suggestion of suppression of urine or of haematuria is a sign for careful watching and, in an established case, for immediate cessation of chemotherapy

Chemotherapy

The drugs of choice are sulphapyridine sulphathiazole or sulphadiazine Minor toxic effects are much less with sulphathiazole and sulphadiazine and they are preferred for out patients, but availability of supply may sometimes hamper choice. It is well known that it is best to establish a good concentration of the drug as soon as possible. The first two days are the most important and the highest dosage compatible with safety should then be given After that a smaller maintenance dose suffices

A high dosage of sulphapyridine is apt to produce nausea, considerable malaise and frequent vomiting in out-patients, hence the recommendation for the first forty-eight hours to be passed in bed In general it is useless to try to give as heavy dosage of sulphapyridine to out-patients as to bed patients and one has to be content with giving out-patients the same dosage spread over a longer period. Sulphathiazole and sulphadiazine are equally well tolerated by bed and out patients.

The high fluid intake so essential for safety from major renal toxicity is much more likely to be maintained in bed patients The fluid intake is most important of all in those engaged on heavy work where they sweat a great deal.

Toxicity and its treatment is fully considered on p. 69.

Sulphapyridine

1 *Bed Patients* Total for course 24 gm.

Day 1 Total 6 gm 1 gm. at 8 A.M., 12 noon, 4 P.M., 8 P.M., 2 gm at 12 midnight

N.B Naturally it will seldom be possible to start at 8 A.M. on the first day of treatment but it is permissible, if only one or two doses have been missed; to distribute them over the remaining time, so that the full 6 gm is administered.

Days 2–5 Total 4½ gm per day ¾ gm. at 8 A.M. 12 noon 4 P.M. 8 P.M. 1½ gm. at 12 midnight.

2 *Combined Bed and Out-patient* Total for course, 27 gm.

Days 1–2 Same as for first day above — total 12 gm. or 6 gm per day Patient in bed.

Days 3–7 Total 3 gm. per day 1 gm at 8 A.M. 2 P.M. and 8 P.M.

3 *Out-patients* Total for course, 23 gm

Days 1–2 Total 4 gm. per day 1 gm. at 8 A.M., 1 P.M. 6 P.M. 11 P.M.

Days 3–7 Total, 3 gm. per day 1 gm. at 8 A.M. 2 P.M. 8 P.M.

Sulphathiazole and Sulphadiazine

Bed patients and out patients are given 6 gm. daily for four days 1 gm. at 8 A.M. 12 noon, 4 P.M. 8 P.M and 2 gm. at 12 midnight.

It is of the utmost importance, particularly in the first two days that the drug should be taken regularly and without omission. It is always best to see patients daily and, if necessary to issue the drug in daily doses to ensure attendance of the patient. In this way it is possible to deal with any toxic effects and to watch progress.

Nausea and vomiting with sulphapyridine are common complaints and are a cause of failure of chemotherapy in some cases. This may be because the drug is vomited or because the patient ceases to take the drug Patients should not be warned of the possibility of sickness, and if a patient starts to vomit in a venereal disease ward, he should be removed at once or an epidemic of vomiting will begin. It is best for patients to crush the tablets before swallowing first, because they are easier to swallow and secondly because sometimes the tablet through some change in the composition of the binder is so hard that it is not absorbed and passes through the intestines unchanged. Patients will often retain the drug better if it is put up as an emulsion

If the patient is genuinely unable to take sulphapyridine,

an immediate change to sulphathiazole or sulphadiazine must be made. Chemotherapy must cease only if there is haematuria suppression of urine or some other very severe reaction

Whatever the system of dosage used it is generally evident after the first forty-eight hours whether the treatment is going to be successful or not. Probably the important chemotherapeutic effect is produced during this time. A high percentage of cases can be cured under certain conditions by even one single massive dose of a sulphonamide. (This is discussed further on p 96)

The progress of the patient should be checked daily by inspection examination of urine and if possible by smear examination The best time to collect the smear specimen is in the morning before the patient urinates An intelligent patient can be instructed how to make a satisfactory smear by drawing a slide over the meatus

A case reacting well begins to dry up quickly and the discharge diminishes rapidly after twenty four hours, may have ceased in forty-eight hours and is generally negligible in seventy two hours A small morning bead of mucus may persist for a few days after this but is unlikely to be serious if the patient has been properly instructed to abstain from squeezing or milking his penis

If smears are examined gonococci are likely to be absent and remain so after twenty four hours The amount of pus in the morning smear gradually diminishes and should be negligible by the end of a week. The urine clears in like fashion haze disappearing by the third or fourth day Some threads and debris may persist for another week or ten days but in the straightforward case will call for no special treatment.

LOCAL TREATMENT

Irrigation

Gonorrhoea can be cured by chemotherapy alone but the best results are generally obtained when local and general treatment are combined This statement is qualified by the proviso that irrigation is done by skilled persons a category which does not include the average patient It is better to dispense with irrigation if the practitioner or a skilled attendant cannot carry out this treatment

In the early case two anterior irrigations with two pints

of a one in ten thousand solution of potassium permanganate daily from the second to the fifth day are indicated, followed by one daily for the next few days if the urine is not quite clear Irrigation may be anterior of the urethra alone, or posterior when the irrigating fluid is allowed to enter the bladder The technique of these procedures is described on page 324. As previously stated a few threads may persist for some time after the disappearance of all other signs and symptoms and are not an indication for prolongation of treatment. These threads seldom indicate a persistence of infection and if the patient is left alone will eventually disappear

A hand syringe compares very unfavourably with irrigation and must not be used if irrigation is available In the hands of a skilled person it does little good and used by the average patient is positively dangerous.

To sum up the early case treated on the foregoing lines will give evidence of a good reaction by about the third day and should be completely free of signs and symptoms within seven to ten days. The case is then ready for observation and testing which will be described fully later (Such a case is illustrated in Case Record I p 20)

SULPHONAMIDE RESISTANCE

A certain number of acute cases namely 5–20 per cent, do not yield to the first attack with chemotherapy At the end of the course the discharge is still present although probably diminishing and the urine is still hazy Frequently gonococci are still present in smears

A careful search must now be made to make sure that no complications, such as prostatitis, vesiculitis or infection of urethral ducts or glands, are present The search must be conducted with due care, for any rough handling of the urethra or prostate can only do harm Prostatic massage and the passage of instruments are absolutely contra-indicated If the investigation shows no gross abnormality it must be concluded that the first effort at chemotherapy has failed Such failures are less common now that the importance of adequate early dosage is realized but were common enough in early days when doses of sulphonamides on an almost homoeopathic scale were used

CASE RECORD I ACUTE UNCOMPLICATED GONORRHOEA (MALE)

A. B. Age 26 Married

History—Extramarital coitus 6 days ago. Marital coitus 2 days ago. 2 hours—discharge and dysuria. No previous venereal disease.

Examination—Yellow purulent urethral discharge. Meatus red and pouting.

Day	Clinical Discharge	Urine	G.C.	P.C.	E.C.	S.O.	Chemotherapy	Irrigation	
1	Pus	1 cloudy 2 clear	+	++++	+		M & B 693, 6 gm.		Bed patient during chemotherapy
	Pus	1 hazy 2 clear	+	++++	++		M & B 693, 4 5 gm.	Pot. permang 1/10,000 twice daily	
3	Mucus	slight haze clear		+++	++		M & B 693 4·5 gm.	Ditt	
4	Nil	clear few threads; clear		++	++		M & B 693, 4 5 gm.	Ditt	Smear specimen taken with loop from fossa navicularis
5	Nil	1 clear few threads; clear		+	++	–	M & B 693, 4 5 gm.	Ditto	Dut
6	Nil	clear clear					Nil	Ditto	
7–9								Ditto, once daily	
	Nil	clear clear					Nil	Nil	
5	Nil	lear clear					Nil	Nil	

Period of Observation

Day	Clinical Discharge	Urine	Prostatic Smear			Prostatic and Vesicular Culture	
	Nil	lear clear		+	+	No gonococci	
28	Nil	clear clear				Ditto	Allowed to resume alcohol
42	Nil	lear clear				Dut	
70	Nil	lear lear				Dut	
9	Nil	clear lear				Ditto	Urethroscopy = no abnormality Cowper's d ez 6 pressed easily W R. = negatn C.F T = nega-tive
98	Nil	lear lea					Returning for result of tests. No evidence of active disease Discharged cured

G.C. = gonococci
P.C. = pus cells
E.C. = epithelial cells
S.O. = secondary organisms

5 to lls per field
so lls and more per field.
W.R. = Wassermann Reaction.
C.F.T. = Complement Fixation Test.

When a particular sulphonamide fails to give a response, it is pointless continuing its use. At the end of the first course in such a case, local treatment continues with irrigations, if possible twice a day and certainly once a day Chemotherapy should not be recommenced under one week, for fear of toxic effects on the haemopoietic system. If at the end of a week of local treatment, signs and symptoms persist, and certainly if gonococci are still to be found in a urethral smear further chemotherapy is indicated A new drug is to be used If sulphapyridine was used on the first course, sulphathiazole or sulphadiazine should be substituted

The majority of initial failures will now react. Local treatment continues throughout.

Fever Therapy

Even better results will be obtained if the second course of chemotherapy is accompanied by fever therapy Fever is easily and safely produced by T.A.B. vaccine, but patients should naturally be in bed preferably under supervision The dosage to be recommended is 25 millions of organisms intravenously on the first day of chemotherapy and 50 millions forty-eight hours later provided the temperature has returned to normal. A third dose of 75 millions can be given in another forty-eight hours if there is not already evidence of a satisfactory response. It is best to have the T.A.B vaccine broken down by a pathologist so that the dose of 25 millions is contained in 1 c.c. In this way the dose is likeliest to be accurate, for the use of a stock vaccine would necessitate the measuring-up of a very small quantity of fluid. The vaccine is best given in the morning

The temperature begins to rise in a half to a few hours and may reach, in the average case, 102 –104 F There are the usual accompaniments of sweating and shivering A half hourly temperature chart should be employed, and if there is any tendency to hyperpyrexia, it can be controlled by tepid sponging and salicylates.

The fever is maintained as long as possible by keeping the patient well wrapped up in blankets and with hot-water bottles.

The fever can be increased by giving another dose of vaccine some four hours after the first. The results with a single dose have proved so satisfactory however that this

CASE RECORD II UNCOMPLICATED SULPHONAMIDE-RESISTANCE (MALE)

C. D Age 30 Single

Gonorrhoea 2 years ago. Treated by M & B 693 and irrigation for 1 month. No relapse Uncomplicated.

History.—Exposure to infection 3 days ago and 2 months ago. Urethral discharge for day

Examination.—Purulent urethral discharge.

Day	Clinical Discharge	Urine	G.C.	P.C.	F.C.	N.O.	Chemotherapy	Irrigation	
1	Pus	1 hazy 2 clear	+	+++	+	–	M & B 693, 6 gm.		Bed patient during chemotherapy
2–5							M & B 693, 4.5 gm.	P.P. b.d. 1/ 0,000	Total, 24 gm. of M & B 693
6	Muco-pus	1 slight haze, 2 clear	+	+++	++			Ditto	
12	Muco-pus	1 hazy 2 clear	+	+++	+			Ditto	Irrigations have continued twice daily
3–6							M & B 760, 6 gm.	Acriflavine 1/ 0,000 b.d.	No evidence of any complication
7	Nil	clear with threads, clear		+				Ditto	Intra urethral smear from fossa navicularis
8–12	Nil							Ditto	
13	Nil				+			Stop	Diet

Period of Observation

Day	Clinical Discharge	Urine	Prostatic Smear	Prostatic and Vesicular Culture	
8	Nil	clear clear			
3	Nil	clear clear		No gonococci grown	Allowed alcohol
49	Nil	clear clear		Ditto	
77	Nil	clear 2 clear		Ditto	
98	Nil	clear 2 clear	+	Ditto	W. R. = negative. C.F.T. = negative. Cotton sound passed easily. Nil abnormal palpable along urethra.
105	Nil	clear clear			Returning for results of tests. Discharged cured

procedure is not recommended. Untoward happenings are very rare and fatalities are almost unknown Naturally pyretotherapy should only be used if the general health of the patient is good. Pyretotherapy is a very valuable method of treatment in many complications of gonorrhoea and is used by some venereologists with excellent results in acute gonorrhoea from the first day In practice it is difficult enough in the first instance to keep the average patient in bed so that it is unlikely to be used as a routine.

A majority of uncomplicated non-reactors will yield to a second course of chemotherapy with or without pyretotherapy but most by the combined treatment a few more days of irrigation will see the urine clear and the patient will now be ready for the routine observation

Should a second course of chemotherapy fail to give results an immediate trial of pyretotherapy is indicated This will clear up a certain number of resistant cases but if not, and provided that there are still no complications, it is permissible to try yet another sulphonamide, or *faute de mieux* return to the first

If a case has got thus far without yielding to treatment, a most searching investigation including examination of prostatic fluid, complement fixation test and instrumentation should be undertaken Generally some focus of infection will be found It is best to precede a third trial of chemotherapy by a red and differential white blood cell count

When available, sulphadiazine is the drug of choice for the third course, but sulphanilamide is sometimes effective, particularly when gonococci are no longer present in the discharge Appropriate dosage with sulphadiazine is 6 gm. daily for four days Sulphanilamide is given in 6-gm. doses for three days, and then in 3-gm. doses for the next four to six days.

Local treatment by irrigation should continue daily throughout, and after the first week it is wise to begin posterior irrigations When gently and expertly done, there is not the slightest danger of spreading infection All but a minute percentage of cases will react to the energetic measures described above The small group still showing signs of activity will generally be found to have some deep-seated focus of infection in the prostate or elsewhere. A very few cases are genuinely resistant to all forms of chemotherapy but will

CASE RECORD III UNCOMPLICATED SULPHONAMIDE-RESISTANCE (MALE)

E. F Age 35 Single

History—Exposure 5 days ago. Discharge for 2 days. Frequency and dysuria.
Examination.—Purulent urethral discharge.

Day	Clinical Discharge	Urine	G.C.	P.C.	E.C.	S.O.	Chemo-therapy	Irrigation	
	Pus	cloudy slight haze	+	++++	–	–	M & B 760, 6 gm.		Treated as out-patient
2–4							Ditto	P P / 0,000 b.d.	Total M & B 760, 24 gm.
5	Muco-pus	slight haze, clear	–	+++	+	+		Ditto	
6–9								Ditto	Slight discharge per meats
	Pus	hazy clear	+	+++	+	+		Ditto	
							M & B 693, 4 gm.	Acriflavine / ,000 b d.	
3–7							M & B 693, 3 gm.	Ditto	Total M & B 693, 3 gm.
8	Muco-pus	hazy clear	+	++++	+	–		Ditto	Investig tion—no evidence of any complication. Prostate and vesicles normal to touch
9	Muco-pus	hazy clear	+	++++	–	–		P P /10,000 b d.	T.A.B. Vaccine 5 million organisms. Fever to 3 F
	Muco-pus	slight haze clear	–	++	+	–		Ditto	T A.B 50 millions. Fever on F
3	Nil	clear with threads, clear		++	++	–		D to	T.A B. 75 millions. Fever to 3 F C F T =negative
28	Muco-pus	clear with thread lear	+	+++	+			Ditto	Investig tion still reveals no clinical evidence of pread from urethra. Blood counts —normal
29–32							Sulphadi zine 6 gm.	Ditto	Total sulphadiazine 24 gm
33	N l	lear with threads, clear	–	++	++	–		Ditto	Intra-urethral smear specimen
40	Nil	lear lea						Stop	

Routine investigations 47th, 54th, 6 st 68th nd 9 h days N gonococci cultured N gonococci or excess of pus in smears

			Prostate Smear	Prostatic and Vesicular ulture	
4	Nil	lear lear		N gonococci	W R – g e. C F T = g Urethroscopy = ne m L Cl sound 26 passed
3	Nil	cle ear			Discharged cured

eventually be cured by local treatment with irrigation

In all resistant cases it is wise to ring the changes on the irrigating fluid, choosing from among potassium permanganate, protargol, mercury oxycyanide and acriflavine. Good results are sometimes obtained by using different solutions for the morning and evening irrigation.

Gonococcus vaccine should also be employed in such cases A course of 8–10 injections given on alternate days is advised The course begins with 125 millions the first dose, 250 millions second dose, 500 millions third and subsequent doses The best vaccine is a polyvalent type containing 500 million organisms per c.c.

The most effective therapeutic agent in cases of sulphonamide resistant gonorrhoea is penicillin (Chapter IX) and it should be used without delay if it is available. In the very rare cases where both penicillin and the sulphonamides are ineffective, hypertherm treatment (p 350) is indicated.

Chapter III

GONORRHOEA IN THE MALE (*continued*)

COMPLICATIONS

Venous Thrombosis

A thrombosis of the dorsal vein of the penis is sometimes seen in acute gonorrhoea The vein can be felt as a hard cord most easily palpable in the prepuce. There may be a little oedema of the prepuce which is dusky in colour More rarely thrombosis may occur in the veins round the spermatic cord in cases of epididymitis No special treatment is necessary for these cases.

Infection of Para Urethral Ducts

A careful inspection of every penis and urethra should show how frequent are minor abnormalities of the glans and urethra Malformations of the meatus, fossae, ducts and crypts of the urethra in and near the glans are all potential sites for infection acute and chronic by the gonococcus They are not quite so important since the use of the sulphonamides but must be remembered and carefully looked for in any case which does not react normally to treatment

These ducts or crypts vary in length from a mere dimple to an inch or more in length Some open on the skin some within the urethra and others communicate with both An extraordinary variety can be described and there is no rule to govern the number direction and shape they may take in any case They are especially common with hypospadias Some of the commoner abnormalities are illustrated (Fig 6) and a very complete description is available in Dr Janet's *Diagnostic et traitement de la blennorragie*

Infection of a duct or crypt may occur but rarely without infection of the urethra or may precede a urethritis The gonococcus may lie dormant in such a situation after urethritis is apparently cured and cause a relapse — or better a re-infection of the urethra — at a later date Treatment of any such focus of infection if there is no reaction to chemotherapy must be radical and complete

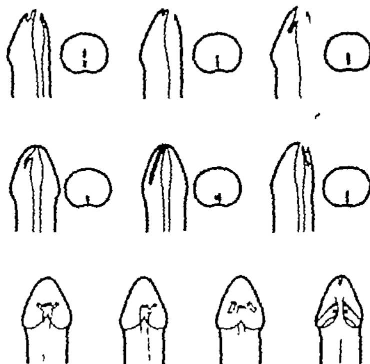


Fig. 6.—Some Abnormalities of the Urethra
Bottom right-hand diagram shows the situation of Tyson's glands at

The length of the duct must be ascertained by probing and it should be laid open completely if possible using the electrocautery. If this is not feasible the electrocautery should be used to cauterize the duct in all its length and to open it up as far as is safe. These operations are most easily performed under anaesthesia with Evipan or Pentothal.

A severe case of this kind occurred in a man with chronic gonorrhoea. The glans was scarred and dotted with small openings through most of which a fine probe would pass into the urethra. Pus containing gonococci could be expressed from these openings and the meatus being pinpoint in size, on urination a fountain display was produced. According to the patient, some of the openings had been present all his life the others having appeared since the onset of the gonorrhoea. The treatment adopted here chemotherapy having no effect,

was to perform a meatotomy and to pass the white-hot cautery along all the ducts, opening them widely. Further chemotherapy was employed, the meatus was kept dilated with sounds and there was no relapse in a three month follow up.

An important type in this class is the so-called Tysonitis. This is not uncommon with acute gonorrhoea and consists of abscess formation on one or both sides of the frenum. From a pinpoint opening pus containing gonococci can be expressed but a frank abscess cavity seldom forms. A probe passed through the orifice can occasionally be introduced into the urethra. Oftener the cavity appears only to communicate with the skin, although its depth varies greatly and the probe sometimes penetrates for astonishing distances in any direction. Possibly, in some cases, the infection spreads outwards from a deep urethral crypt, but more commonly the infection is external in a sebaceous parafrenal gland. The condition is treated by cauterizing deeply and widely with the electrocautery.

Littritis

Infection of the small urethral glands of Littré is to be considered in investigating acute and subacute cases not responding rapidly to treatment. Infection of these glands is often preceded by rough handling of the penis by patient or doctor in an effort to produce a discharge at the meatus.

The urine in such cases is often clear but contains numerous small threads. Discharge is usually present, but may only be noticed in the morning before urination. The presence of the condition may be diagnosed by gentle palpation of the urethral wall against a straight sound passed down the urethra. Infected glands are palpable as small hard seeds between finger and instrument. The urethroscope may show inflammation of the mouths of the ducts, and pus may be seen to exude after gentle pressure on the urethra. Naturally any instrumentation is carried out only after any acute urethritis has been dealt with by local and general treatment and the urine is clear.

Treatment by irrigation alone is often enough, but massage of the nodules over a straight sound twice weekly is necessary in some cases. Treatment is controlled by examination of urethral discharge produced after instrumentation. If the gonococcus is still present, further chemotherapy, preferably

combined with T.A.B fever therapy is indicated in conjunction with, or after local treatment.

Peri Urethral Abscess

Complete occlusion of the mouth of the duct of an infected gland may result in abscess formation anywhere along the urethra. The size of the abscess varies but may be as large as a plum, particularly when situated at the perineal end of the anterior urethra.

The complement fixation test is positive in about 80 per cent of such cases according to the statistics of the London Lock Hospital Research Unit.

Peri urethral abscess is generally palpable as a hard tender swelling and the patient complains of pain, increased on passing urine. Retention of urine is uncommon with abscess of the penile urethra. A low fever is common. Any urethral discharge may dry up as these symptoms appear. The urine may be clear if acute urethritis has subsided under treatment.

Local treatment consists of rest with frequent hot baths irrigations and local heat. Sedatives are indicated. The abscess may subside with simple treatment, but usually it points either into the urethra or externally. Passage of a straight sound, provided the urine is clear will assist diagnosis and may cause the abscess to rupture and discharge into the urethra. Urethroscopy sometimes shows the abscess bulging into the urethra and an opening may be attempted by the use of a small knife through the cannula of the urethroscope. This manoeuvre is rarely necessary for most abscesses pointing internally will rupture spontaneously with local treatment.

Rupture into the urethra is followed by a purulent urethral discharge and relief of pain. Chemotherapy is now begun and anterior irrigation continues. When discharge has ceased, bi-weekly massage of the urethra over a straight sound for a few weeks is advised. When the abscess points to the outside, it should be opened widely under general anaesthesia, nitrous oxide or Evipan. A straight sound in the urethra is a good tether and guide and the incision should be in the line of the urethra. A little urine may leak through the wound for a few days after operation but fistula formation is very rare.

A gauze pack is inserted and the wound allowed to granulate. Treatment of abscess along the urethra by aspiration

never gives results comparable with those obtained by open operation The follow-up of any perineal abscess case must include careful watching to ensure that healing does not lead to stricture formation.

Cowperitis

Acute infection of Cowper's gland usually occurs early in a gonorrhoea. It is characterized by perineal pain on urination and possibly on defaecation and occasionally by acute retention of urine There is generally some fever and general malaise. The urine may show some turbidity or if the urethritis has been controlled may be clear or contain only a few threads One or both glands may be affected

The gland can best be felt between the forefinger inserted into the rectum and the thumb laterally placed on the perineum When the gland is inflamed a hard tender swelling is felt ranging in size from a pea to a marble. If an abscess forms there is usually an obvious dusky swelling in the perineum very tender to the touch.

Some acutely inflamed glands will subside with local treatment by heat in the form of baths and fomentations. The majority go on to abscess formation When fluctuation appears the cavity is opened widely under general anaesthesia packed or drained and allowed to granulate. A straight sound in the urethra is a useful guide in making the incision which should be parallel with the urethra A little leakage of urine through the wound after operation is common Fistula after operation is rare but is more liable to occur should an abscess be left to burst on its own Irrigation may continue throughout and further chemotherapy may be indicated Such cases should have careful and prolonged follow up to exclude possible stricture formation

Chronic infection of one or both glands may be responsible for some cases of persistent gleet or for relapse, but this is apparently not common. The glands should always be palpated in doing a prostatic examination or massage If a chronic infection is suspected as evidenced by a slight urethral discharge and a small hard tender and palpable Cowper's gland or glands, treatment will be by massage of the gland between finger and thumb two or three times a week, with posterior irrigations once or twice daily To this may be

added chemotherapy Most chronic cases will yield to this treatment, but a few may be stimulated into acute inflammation and require surgical intervention as described above.

Peri Urethritis and Chordee

Sometimes the peri urethral tissues of the penile urethra become generally infected without actual abscess formation. Rarely is the condition enough to produce marked signs or symptoms In the most pronounced form a spread into a corpus cavernosum may produce a very painful condition known as chordee The infiltration of the tissues tends to produce erection of the penis and at the same time interferes with the blood flow and the penis is crooked, bent towards the affected side.

Strong sedatives and hot and cold applications are indicated. Sometimes the greatest relief is obtained by spraying the penis with ethyl chloride.

Chordee is a much more important condition than the nocturnal erections of acute gonorrhoea and needs more treatment and a closer follow up While external evidence of peri urethral infection, apart from chordee, is wanting instrumentation may reveal a varying degree of difficulty in passing a sound through the affected part of the urethra, and urethroscopy will show a loss of the normal elasticity and inflatability over the corresponding part of the urethra.

Apart from the general treatment of the urethritis in such cases, the local condition must be treated by frequent instrumentation during the normal period of observation and at intervals for six months or a year afterwards in order to avoid any possibility of stricture formation

Prostatitis (General Description)

(1) *Examination of the Prostate* The prostate gland can be palpated with the patient in a number of positions He may be lying on his back in the lithotomy position — a method favoured by the French — or more simply he can be examined in the knee-elbow position on a couch or bending over the back of a chair with legs apart. The well lubricated forefinger is gently introduced well into the rectum, no pressure being put upon the prostate The lubricant employed may be one of the proprietary jellies or plain Vaseline

Gently running the finger over the surface of the prostate, it can be appreciated in the normal subject that the gland is elevated on either side of the midline and depressed in the centre The normal gland feels firm and elastic and is not tender to touch

A great enlargement tenderness or areas of softness are suggestive of acute prostatitis or prostatic abscess A little enlargement with possibly a rather nodular feeling will suggest a subacute or chronic infection

Above the prostate on either side can often be felt the seminal vesicles. When healthy they are quite soft, or even impalpable, and never tender Only experience can teach the finer details of rectal examination but anyone, having felt the normal prostate a few times should be able to distinguish the grosser abnormalities

(2) *Prostatic Massage* Prostatic massage is intended to evacuate the gland ducts of the prostate and to promote drainage. In massage the beginner should remember that no harm can be done by gentleness, but that rough usage is an incentive to the spread of infection in the prostate and beyond Massage will generally include the seminal vesicles as well as the prostate

No massage of the prostate or vesicles should ever be undertaken until all signs of acute urethritis have disappeared and until at least fourteen and better twenty-one, days have elapsed from the beginning of treatment

The actual technique consists of a downward and inward pressure of the finger over the vesicle and prostate about a dozen times on each side Finally the central depression is massaged a few times If desired the extruded prostatic and vesicular fluid which is now present at the meatus or can easily be milked along the urethra can be examined by smear or culture Massage should always be followed by a posterior irrigation.

If it is desired to culture the prostatic and vesicular fluid the urethra should be irrigated beforehand with sterile water

Urine passed after a prostatic massage may be opalescent or even cloudy and contain threads and debris This in conjunction with a two-glass urine test done before the massage can be used as a method of assessing the state of the prostate

gland and is sometimes known as the three-glass urine test. It is not a particularly accurate method of assessment.

The interpretation of smears made from the prostatic and vesicular fluid is sometimes difficult. If gonococci are found in the smear it is obvious that infection is still present and that further treatment is indicated but when the smear shows only a varying amount of pus and epithelial cells interpretation is not always easy

It is the common practice to employ the signs + ++ +++ ++++ to indicate the number of cells present in a smear + means five to ten cells per microscopic field, ++ ten to fifteen, +++ fifteen to twenty and ++++ twenty and over It is obvious that the vigour of the massage and the method of spreading fluid upon the microscope slide may influence the reading of a result in any given case. Pathological results of this kind, therefore, must be carefully correlated with clinical findings when deciding on the advisability or otherwise of treatment, and the system of allowing the number of + signs on a pathologist's report to be the final guide to the necessity for continuing or discontinuing prostatic massage is not to be recommended

A finding of + or ++ is not alarming in a prostatic smear in the follow up of an uncomplicated case of gonorrhoea, but ++++ at any time in the absence of clinical signs would be an indication for a close watch and an increase in the number of tests A similar finding after a known prostatitis would indicate the need for further treatment only if the amount of pus should show no signs of diminishing in subsequent examinations.

The patient and not the pathological report, is the index for treatment. It should be remembered that the average case of gonorrhoea will do much better untreated rather than over-treated, in respect of mechanical interference.

(3) *General.* Infection of the prostate gland is one of the commonest complications in gonorrhoea and is the associate and forerunner of other complications The gland is probably potentially infected in every case, gonococci lying in the mouths of the ducts but with early energetic treatment, particularly since chemotherapy has been available, clinical involvement of the gland can usually be avoided. To avoid infection of the prostate, the most important thing is to avoid unnecessary

interference. Prostatic investigations are contra indicated in acute gonorrhoea unless there is good reason to suspect an acute prostatitis or abscess

Prostatic massage must never be done under fourteen days from the start of treatment is seldom necessary under twenty one days and should only be performed in the absence of any evidence of acute infection of urethra or prostate gland In no department of medicine is masterly inactivity so likely to be a success as in acute gonorrhoea. Stick to chemotherapy and gentle irrigation and the vast majority of patients will quickly recover Traumatize the urethra and prostate by finger or instrument and complications are assured

The longer a patient hesitates before seeking advice, the more likely is he to get a clinical prostatitis Prostatitis may supervene in a case under treatment, but is not likely if the above precepts are followed Infection may linger on in the prostate after a clinical cure, the patient showing no signs or symptoms, but remaining potentially infectious and liable to relapse Quite often a chronic infection of the prostate following an uncured or untreated gonorrhoea is the cause of gleet

Acute Prostatitis

This is commonest in acute or subacute gonorrhoea but may sometimes be superimposed on a chronic prostatitis The urethritis may be untreated or signs of prostatitis may appear after treatment has started Very often a cessation or diminution of the urethral discharge precedes the first symptoms by twenty four hours or so There is general malaise, the temperature rises to 103 104 F and there is frequency of urination dysuria and often pain in the perineum The urine is cloudy in both glasses by the two-glass test Rectal examination reveals an enlarged tender prostate. The enlargement may be more pronounced on one side or the other The complement fixation test in such cases is usually strongly positive

Treatment If general treatment has not started the routine for an acute urethritis should begin at once The patient must stay in bed The bowels must be kept well open An alkaline mixture with hyoscyamus helps to allay the dysuria Frequent hot baths are given Hot rectal douches can also be used and hot applications or bottles on the perineum are soothing

A quarter-grain morphia suppository may be necessary in the early stages

Irrigation twice daily can begin as soon as the acute symptoms have subsided At first, anterior irrigation may only be possible, but if bladder washes can be given, there is no objection and in any event they should begin as soon as possible. Irrigation is absolutely contra indicated if it is not to be done by expert hands.

Symptoms should subside in the course of a few days and the urine should begin to clear All being well, the prostate need not be palpated again until 7–10 days after the first examination By this time it should in the average case have lost its tenderness and have subsided markedly Treatment will continue with irrigation Massage will not be begun under another fourteen days, and then only if it is certain that no acute inflammation remains. Further treatment is as for subacute prostatitis to be described later

Prostatic Abscess

Acute prostatitis may in spite of treatment, progress to abscess formation. Symptoms and signs are similar to those of acute prostatitis, but more pronounced Temperature is often higher up to 105 F., and rigors may occur Urinary difficulties are greater and retention is not uncommon The prostate is felt per rectum, to be much enlarged, up to the size of a tangerine orange, and very tender

Treatment The patient is kept in bed and it is wise to administer an enema at the start. Retention of urine is treated by frequent hot baths and by the administration of a quarter grain of morphia by injection or by suppository

If this is not effective in a few hours and the bladder is very distended a medium-size Jacques rubber catheter is passed after preliminary cleansing of the urethra by irrigation and the urine is drawn off Recatheterization is seldom necessary and the use of gum elastic or metal catheters is never called for Chemotherapy will be employed if necessary and gentle anterior irrigations twice daily with potassium permanganate are useful when given by expert hands

Expectant treatment is employed in the hope, usually realized, that the abscess will burst into the urethra When this happens the symptoms rapidly subside and the urethral

discharge reappears. Treatment now continues with irrigation etc., as in a subsiding acute prostatitis. Rarely the abscess may burst into the rectum and in the past surgical approach to the abscess through this channel was sometimes used. This result by accident or design is to be avoided owing to the danger of infection of the rectum with gonorrhoea or of a pyogenic prostatic infection spreading up from the rectum.

Urinary fistula may result when the abscess points into the rectum or into the perineum. Rupture through the prostatic capsule and tracking of the pus into the perineum with formation of a perineal abscess is also rare. Should this happen the abscess is opened under general anaesthesia and a good drainage established. All loculi should be opened with the finger and the track up to the prostate bared and drained. After-treatment in such a case will include careful check on the viability of the urethra.

Surgical Treatment. Should expectant treatment fail in the course of two or three days to produce the hoped for rupture into the urethra, or should there be signs of rupture into the rectum or perineum, then it is best to open the abscess surgically. The perineal route is best. Rectal incision or instrumentation of the urethra are not advised. Under general anaesthesia a crescent-shaped incision with its centre an inch in front of the anus is made. The left forefinger is now introduced into the rectum as a guide and the left thumb retracts the anterior lip of the anus. Pushing up now in the middle line using finger or sinus forceps, the capsule of the prostate is reached and opened at a depth of up to two inches. The right forefinger is used to explore the cavity and break down loculi. A rubber drain is inserted and shortened daily. Healing is rapid. The case is now treated as one of resolving acute prostatitis.

Subacute Prostatitis

After acute prostatitis or prostatic abscess the gland passes through a stage of subacute inflammation on the way to recovery. Subacute prostatitis may also arise *de novo* in the course of a gonorrhoea. The prostate is a little enlarged and tender and the sym[illegible] are discharge and frequency of urination. The uri[illegible]ally cloudy or hazy. The complement fixation tes[illegible]lly positive

CASE RECORD IV SUB-ACUTE PROSTATITIS

G H. Age 30 Single

History.—Acute gonorrhoea, uncomplicated, treated as out-patient with 24 gm. of sulphadiazine in 4 days, and potassium permanganate irrigations t the oth day

Day	Discharge	Urine	G.C.	P.C.	E.C.	S.O.	
7	Nil	clear 2 clear					
21	Muco-pus	clear with threads, clear	+	++++	+	+	Complaining of morning discharge. Prostate little enlarged, and tender
			Prostatic Smears				
22–25	Nil		+	++++	–	–	1 gm. M & B 760 six times daily Total, 24 gm. Prostatic massage twice weekly Daily irrigation
29	Nil	clear 2 clear		+++	+	+	C.F T.= weakly positive (±)
30–60	Nil						Prostatic massage twice weekly irrigation after massage
61–88	Nil	clear clear					Prostatic and vesicular smears and cultures weekly N gonococci and no excess of pus cells in smears
0e and 6							Prostate and vesicles normal. Negative tests, as above
142							c.c. polyvalent gonococcus vaccine, 900 million or ganisms per c.c., injected
44	Nil	clea clear	–	+	++	++	Prostate and vesicles clinically normal. Culture = no gonococci grown. W.R. = negative. C.F T = negative. Urethroscopy = normal. Clutton sound 22/26 passed easily
51	Nil	clear clear					Discharged cured

discharge reappears Treatment now continues with irrigation etc., as in a subsiding acute prostatitis Rarely the abscess may burst into the rectum and in the past surgical approach to the abscess through this channel was sometimes used This result by accident or design, is to be avoided owing to the danger of infection of the rectum with gonorrhoea or of a pyogenic prostatic infection spreading up from the rectum.

Urinary fistula may result when the abscess points into the rectum or into the perineum Rupture through the prostatic capsule and tracking of the pus into the perineum with formation of a perineal abscess is also rare Should this happen the abscess is opened under general anaesthesia and a good drainage established All loculi should be opened with the finger and the track up to the prostate bared and drained. After-treatment in such a case will include careful check on the viability of the urethra

Surgical Treatment. Should expectant treatment fail in the course of two or three days to produce the hoped for rupture into the urethra or should there be signs of rupture into the rectum or perineum then it is best to open the abscess surgically The perineal route is best Rectal incision or instrumentation of the urethra are not advised Under general anaesthesia a crescent-shaped incision with its centre an inch in front of the anus is made The left forefinger is now introduced into the rectum as a guide and the left thumb retracts the anterior lip of the anus. Pushing up now in the middle line using finger or sinus forceps the capsule of the prostate is reached and opened at a depth of up to two inches The right forefinger is used to explore the cavity and break down loculi A rubber drain is inserted and shortened daily Healing is rapid The case is now treated as one of resolving acute prostatitis

Subacute Prostatitis

After acute prostatitis or prostatic abscess the gland passes through a stage of subacute inflammation on the way to recovery Subacute prostatitis may also arise *de novo* in the course of a gonorrhoea The prostate is a little enlarged and tender and the symptoms are discharge and frequency of urination The urine is generally cloudy or hazy The complement fixation test is generally positive

vided any discharge has ceased. Chemotherapy will also be employed. Progress is checked on the clinical signs, by examination of prostatic fluid and by the diminution of its pus cell content, by disappearance of gonococci in smear and culture and by the reversal of the complement fixation test to negative. Smears should be examined weekly if possible during treatment, and cultures taken at the end of courses of massage. The complement fixation test need only be repeated at intervals of eight weeks.

If a second or subsequent course of massage is indicated an interval of 10–14 days should be allowed to elapse before resuming treatment. During this time daily irrigation can continue if necessary and a course of injections of a polyvalent vaccine may begin. When the clinical signs have returned to normal and pathological findings are satisfactory a routine follow up is undertaken. More will be said on this subject in dealing with metastatic complications.

Seminal Vesiculitis

The state of the seminal vesicles follows very closely that of the prostate, but occasionally an acute or chronic vesiculitis may appear to be a solitary phenomenon. Acute vesiculitis is ushered in with fever, frequency of urination, dysuria and terminal haematuria, the urine being cloudy.

The affected vesicle, or vesicles, is palpable, enlarged and very tender. Treatment and follow-up are on the same lines as for acute prostatitis. In chronic vesiculitis the vesicle is felt to be hard and fibrous. Treatment is the same as is used in a chronic prostatitis and the two conditions are generally coincident.

Direct operative interference with the vesicles or attempts to promote drainage via the vas deferens are absolutely contraindicated. All cases of vesiculitis will respond in time to chemotherapy, irrigation and massage.

Epididymitis

Epididymitis generally arises soon after infection and may even coincide with the onset of symptoms of urethritis. It is commonly unilateral but may be bilateral. It is commonest in the untreated case and should be an extreme rarity after treatment has started.

Chemotherapy is employed and local treatment is by posterior irrigations twice daily When the prostatic swelling and tenderness have subsided discharge has ceased and the urine is clear gentle prostatic massage twice weekly may begin. The massage is given in courses of six with an interval of fourteen days between courses Massage is discontinued when clinical evidence of infection has disappeared and when examination of the prostate fluid by smear and culture shows an absence of gonococci and signs of diminution in pus cell content

Chronic Prostatitis

This condition may be a gradual development in a treated or untreated case or it may follow subacute or acute prostatitis Symptoms may be very slight or none at all the condition being discovered during routine follow up of an acute case or during routine investigation of a complicated case such as arthritis or epididymitis Chronic gleet is sometimes responsible for bringing the patient under observation

The signs are a urethral discharge mostly in the morning a clear or slightly hazy urine containing threads, and a prostate which may feel slightly enlarged and irregular or nodular

The discharge, when present, contains pus cells and possibly gonococci The prostatic fluid examined after massage also contains pus probably in quantity designated as + + + + or + + + and possibly gonococci. Gonococci may be grown in culture even when not found by direct examination

Chronic prostatitis is a condition in which the use of cultures in diagnosis is most important If a culture is to be *made the anterior urethra should be washed with sterile* water before the massage and the expressed fluid dropped directly from the penis on to the surface of the medium contained in a Petri dish. For best results the medium should be at body temperature and returned to the incubator at once

The complement fixation test is often positive sometimes strongly positive in these cases The London Lock Hospital Research Unit quotes a figure of 76 per cent positives in cases of prostatitis

Treatment This should consist of bi weekly massage in courses of six with daily posterior irrigations for the first fourteen days and subsequently after prostatic massage pro-

CASE RECORD V EPIDIDYMITIS

G H Age 22 Single

History.—Exposure 1 days ago. Slight urethral discharge for 6 days. Dysuria. Pain in right groin.

Examination.—Purulent urethral discharge. Right epididymis tender but not swollen.

Day	Discharge	Urine	Urethral Smears G.C.	P.C.	E.C.	S.O.	Chemotherapy	Irrigation	
	Pus	cloudy cloudy	+	++++		–	M & B 760 6 gm.		Right epididymis swollen on 2nd day. Bed, support for scrotum, Antiphlogistine locally
4							Ditto, 6 gm.	P.P 1/10,000 b.d.	Veganin tablets as required. Seconal, ½ gr. at night.
[illegible]	Muco-pus	slight haze, clear						Ditto	
	Muco-pus	slight haze, clear		++	++			Ditto	Swelling subsiding. Allowed up. Suspensory bandage
7	Nil	clear with threads, clear						Ditto once daily	
			Prostatic Smears						
	Nil	clear clear		++++	+	–		Ditto	Prostate slightly enlarged and tender
[illegible]									C.F.T. = strongly positive (++)
									Prostatic massage twice weekly followed by irrigation
	Nil	clear 2 clear		++	++				Prostate and vesicles clinically normal. Epididymis normal
[illegible]		Weekly prostatic and vesicular smears and cultures. No gonococci seen or cultured. No excess of pus							C.F.T. weekly positive (±) on 70th day
[illegible]		Routine Tests							
[illegible]	Nil	clear clear		+	++				Prostatic and vesicular cultures no gonococci. W.R. = neg. i.e. C.F.T. = negative. Epididymis = normal. Urethroscopy = normal. Clutton's sound 22/26 passed easily
55	Nil	1 clear clear							Discharged cured

This complication may be preceded by too early instrumentation or prostatic massage Epididymitis is not very common in chronic gonorrhoea unless there is a previous history of the same condition It would appear that one attack predisposes to another if the sufferer should contract gonorrhoea again

The infection spreads directly from the urethra along the vas deferens A previous or coincident infection of the prostate and vesicles is the rule Violent exercise may be a predisposing cause Epididymitis is often preceded by a diminution or cessation of urethral discharge There is some fever in the early stages, persisting until the swelling is at its height and then subsiding Local pain is the rule and there is often referred pain in the groin and corresponding side of the lower abdomen

The epididymis itself is swollen and very tender There is often some indication of an accompanying prostatitis and vesiculitis. The urine is generally hazy The complement fixation test is positive in the majority of cases of gonorrhoeal epididymitis

For about forty-eight hours from the onset of the swelling the epididymis continues to enlarge and the pain to increase or persist The swelling in some cases is very large, as big as an orange and is always exquisitely tender

General treatment consists in confining the patient to bed on a light diet and it is wise to administer an enema at the start Chemotherapy is used if treatment on general lines has not already begun. Anterior irrigation can begin when swelling starts to subside

Locally the scrotum is supported on a small pillow or towel between the legs Hot applications of Antiphlogistine are renewed as often as necessary A sedative such as Seconal 1½ grains, is needed at night and Veganin tablets can be given as required in the day time In the very worst cases a quarter grain of morphia may be necessary on one occasion at the start. A large variety of drugs and operations, ranging from intravenous sulpharsphenamine to sticking needles into the already painful epididymis, have been put forward in the past as specifics for stopping pain and reducing the swelling They are all unnecessary

Mr J J Abraham surgeon at the London Lock Hospital has pointed out that in the vast majority of cases the swelling

from the start, should, if gonorrhoea is excluded be suggestive of an infection with the tubercle bacillus and a full pathological and surgical investigation must be arranged

Cystitis

The bladder is very rarely infected by the gonococcus. The symptoms are the same as in any other form of cystitis with frequency dysuria and a very turbid urine. A smear of deposit from a catheter specimen shows gonococci Treatment is by chemotherapy and bladder irrigations.

A little frequency and hazy urine persisting after an acute gonorrhoeal urethritis is sometimes due to a mild *bacillus coli* cystitis It yields rapidly to treatment with mandelic acid should sulphonamides fail Pyelitis and pyelonephritis, ureter and kidney pelvis infection by the gonococcus may occur but are excessively rare The diagnosis is made by finding the organism in the urinary deposit taken by ureteric catheter Sulphonamide treatment is indicated.

FOLLOW UP AND TESTS FOR CURE

For safety and to exclude the possibility of relapse, clinical or pathological every case should be followed up at intervals for a minimum period of three months before a final test of cure is made

Clinical relapse in early cases treated by chemotherapy occurs soon after active treatment ceases, usually under one month, and the follow-up visits should be most frequent during this time. After three months of careful investigation, the average uncomplicated case can safely be discharged cured. The three-month limit has another application, for if at the end of this time there has been no clinical evidence of syphilis and if the Wassermann reaction is negative, the possibility of a double infection at the outset can be excluded.

The scheme laid down here is what should be aimed at. In practice, it is rare that the patient will be found willing or able to co-operate to this extent The average patient with gonorrhoea has a short memory and if his discharge has ceased he is very apt to forget his obligations to himself and to the community

and pain increases for forty-eight hours At the end of this time defervescence begins, pain ceases and the swelling starts to subside. Any treatment tried out at the forty-seventh hour is bound to be a great success.

The patient should be kept in bed until he is free from pain the temperature is normal and the swelling has been reduced to something approaching the normal that is from five to ten days Irrigation will then continue twice daily A suspensory bandage should be worn and all exercise for bidden When the urine is quite clear and all acute activity in the epididymis seems settled the prostate and vesicles can be investigated

Clinical signs of prostatitis are generally found and a course of massage of prostate and vesicles should be carried out in every case. Recovery is generally rapid and the few cases which are still not resolving can be hastened by the use of T.A B fever therapy two or three bouts using 25, 50 and 75 millions of organisms by intravenous injection at forty-eight hour intervals By the end of a month all that should be left is a little thickening or hardness at one or other pole, and by the time the observation period is over this, too will have gone. The routine follow-up and test of cure will begin when the prostate and vesicles have returned to normal and the condition of the epididymis is stationary

Pus formation is rare and *bacillus coli* is the organism most commonly found in the pus on these occasions One should be careful of the diagnosis in the case of a man pre senting himself with an epididymitis but with little or no urethral discharge and a clear or only slightly hazy urine In such a case the infection may be gonococcal or it may be due to a pure *bacillus coli* infection It should not be diagnosed as gonorrhoeal without the gonococcus being found in smear or culture The complement fixation test is a good guide in difficult ases being positive in 70 per cent of cases due to gonococcal infection according to London Lock Hospital figures.

A positive diagnosis of gonorrhoea however should only be made if the gr ococcus is found in smear or culture If the epididymitis i due to a *bacillus coli* infection an elaborate follow up is unnecessary An acute epididymitis which is slow in resolving or a condition which is subacute or chronic

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The tests to be described are of a standard only obtainable in special circumstances but as many as possible should be done. Facilities for cultures are not readily accessible every where but an attempt should be made to have cultures even if it is only at the time of the final test. The patient can always be sent to a specialist venereologist or to a venereal disease pathologist if no local facilities exist.

When active treatment is completed the patient is instructed to report for tests after one week provided he remains symptom free.

First Test after One Week The patient is fully examined for clinical signs of disease Any urethral discharge is examined microscopically The urine, which should have been held for at least two hours is examined by the two-glass test A few small threads or flocculi in a clear urine in the absence of any symptoms or other clinical signs of disease need cause no alarm The prostate and vesicles are gently massaged and the expressed fluid is tested by smear examination and if possible by culture. If no abnormality is found the patient is told to report in seven days time

Second Test after Two Weeks The procedure is the same as at the first test If all is well the patient is told he may drink alcohol Alcohol is probably the best provocative test for cure always provided that the patient has abstained completely during the preceding period. Relapse after alcohol generally occurs within forty-eight hours and if the patient does not relapse within this period future tests are almost certain t be negative.

Dr Jules Janet goes so far as to say that he would allow a patient to marry forty-eight hours after a negative alcohol test A satisfactory result from the alcohol test must not be taken to mean that further investigation is unnecessary

Third Test after Four Weeks and Fourth Test after Eight Weeks Repeat first test

Fifth, Final T st after Twelve Weeks This includes general examination inspection of urine and examination of prostate and vesicular fluid by smear and culture A specimen of blood is taken for Wassermann reaction and complement fixation test A urved steel sound the largest that will go through the meatus is passed to the bladder to exclude stricture and the urethra i palpated over the sound Urethroscopy

may be done if an instrument is available, but in the majority of cases yields no more information than does the sound.

The patient should be told to return on an appropriate day to hear the results of his tests and on this last visit the urine should be examined to see whether the instrumentation has stirred up any latent focus If the patient has passed through all these tests he can be regarded as cured

It is always wise to advise a condom for three months after intercourse is resumed because coitus may reveal some undisclosed infection. Further it seems that for some months after gonorrhoea, patients are more liable to pick up banal infections producing non-gonococcal urethritis, and a condom is full protection.

In the straightforward case which reacts at once, no concern need be felt if some of the pathological tests in the first four visits have to be omitted Even if they are not done, however the patient should be seen the urine examined and the prostate and vesicles palpated The final tests are all essential and without them a definite statement cannot truthfully be given to the patient

The use of a vaccine as a provocative at test of cure makes this test even more searching 1 c.c of a polyvalent gonococcus vaccine containing 500 million organisms per cubic centimetre is given forty-eight hours before the pathological tests are conducted The vaccines may have the effect of stirring to activity some latent focus of infection and this would be revealed in the tests Provocative tests, involving the instillation of chemical irritants into the urethra, are dangerous and unnecessary Special consideration and long observation will be given to cases where there has been any abscess formation along the urethra. Instrumentation either for test or for treatment, will be done before the fifth test and carried on after other investigation has ceased In the absence of any evidence of narrowing of the urethra, visits three and six months after the fifth test will suffice.

The finding of gonococci at any test will be a sign for full investigation and a fresh start of treatment A large number of pus cells (++++) in prostatic smears in consecutive tests, even in the absence of clinical signs, calls for investigation and for an increase in the frequency of the tests until it has been decided whether prostatic massage is necessary It is wise in

such cases to have culture examinations as well

During follow-up the finding of an excessive quantity of pus cells in prostatic smears on three consecutive occasions would call for local treatment by a course of three weeks bi weekly prostatic massage Further investigation would follow but the total time of observation would not necessarily be increased.

Investigation of cases presenting no signs of acute gonor rhoea but which have signs or symptoms possibly referable to a gonococcal infection past or present should have repeated investigations on the lines suggested for the final test A positive complement fixation test in a suspected case may sometimes at first be the only evidence of a possible gonococcal infection still remaining The object of investigation should then be to find the site of the closed infection the prostate and vesicles being most suspect The finding of a negative complement fixation test in a rheumatism suspected of being due to a latent gonococcal infection is enough to dispel suspicion

RELAPSE

Relapse is very often due to a too early indulgence in alcohol hence the value of alcohol as a provocative

Any return of acute symptoms and signs occurring more than a month after active treatment has ceased should be viewed with suspicion and is more likely to be reinfection than relapse Clinical relapse when gonococci are present in the urethral smear will be treated on the same lines as a fresh infection but every effort will be made to find out where the gonococci were hidden so that the accident may not occur again It is wise to use a sulphonamide different from that originally used A relapse will very often be found much more resistant to treatment than a fresh case.

Pathological relapse the finding of gonococci by smear or ulture during the period of follow up will require local and general treatment The prostate and vesicles are very often infected in such cases. When treatment of a relapse is complete the ubsequent follow up is again for a full three months The case should be seen weekly for the first month fortnightly f r the sec nd month and finally at the end of the third m nth

REINFECTION

Gonorrhoea confers no lasting immunity but it sometimes seems that the severity of the infection diminishes with each succeeding attack. It has been noted that if a patient has been resistant to any particular drug in one attack, it will not be likely to succeed in another Further complications in one attack often mean complications in the next. This is particularly so in the case of gonorrhoeal arthritis, and in some cases a second attack is very severe and crippling

FATE OF UNTREATED GONORRHOEA IN THE MALE

Gonorrhoea in the male can be classified as a self limiting disease. Until irrigation came into use, most gonorrhoeas were virtually untreated but the majority of patients managed to survive. The *laissez couler* school of French venereologists in the past were content to leave the cure to nature.

Without treatment the purulent discharge of acute urethritis persists for one to three months and then gradually diminishes in quantity becomes serous or mucoid and finally disappears save perhaps in the morning Complications apart, the sufferer is usually restored to apparent normality in six months This happy ending is not the rule. Acute epididymitis and prostatitis are common and chronic infections of para-urethral ducts, the prostate, etc. nearly always result. Stricture of the urethra, now becoming a rarity was commonly seen in days gone by when gonorrhoea was treated with balsamics such as sandalwood oil.

When a long untreated case reports in the subacute or chronic state, the sulphonamides should be used as in acute urethritis, and complications treated individually Fever therapy with a sulphonamide is particularly useful if resistance is encountered

SECONDARY (NON-GONOCOCCAL) INFECTION

The finding of other organisms, for example staphylococci streptococci or *bacillus coli*, besides the gonococcus in a urethral discharge, is common Often they have no obvious effect upon the progress of the disease under treatment but some

essential in women for a much higher percentage of positive results will be obtained by the use of both smears and cultures than by smear examinations alone. The complement fixation test is also important, for a positive test will spur the investigator to seek more definite evidence of infection

If negative findings are obtained at the first test, the examination must be repeated not once but many times In chronic cases positive results are most likely to be obtained just after a menstrual period when gland secretion is most active. A woman suspected of harbouring the gonococcus should not be considered free from suspicion unless a series of tests over at least three months has proved negative.

Chronic asymptomatic or latent gonorrhoea in women is a much commoner condition than in men The gonococcus can remain for years, particularly on and about the cervix, and women so affected are potentially dangerous Sometimes a man may cohabit with such a woman for months before he is infected The danger of infection from these women is greatest near the time of the menstrual period when the active glands are pouring out their secretions and with them gonococci A bout of alcohol too may cause the gonococcus to emerge and infect a partner

In women more than in men each successive attack of gonorrhoea tends to become less severe and Janet believes that a state of relative immunity is achieved by some prostitutes This would explain the relatively small number of infections contracted from prostitutes particularly those taking hygienic precautions between clients Female anatomy is such that a woman unlike a man will contract gonorrhoea the first time she is exposed to infection and it also makes prophylactic measures difficult and unlikely to succeed

Complications of gonorrhoea are more severe and more dangerous in women and the possibility of a prolonged effect upon the general health is greater than in men Sterility rare in the male is not uncommonly due to gonorrhoea in women.

The female genital tract offers immense scope to the gonococcus which exploit the possibilities to the full if permitted Fortunately the advent of the sulphonamides has made the chance of rapid cure very much better at any stage of the disease

ANATOMY

The female external genitals, or vulva, include the mons veneris, labia majora and minora, clitoris, external urinary meatus and vaginal orifice (Fig 7)

From the mons veneris, the eminence in front of the pubis, extend backwards, on either side, the labia majora, which rejoin posteriorly. in the perineum. Externally they are covered with hair internally they are smooth and contain numerous sebaceous glands

Between and partially hidden by the labia majora, lie the labia minora. The labia minora are two folds extending backwards from the clitoris round which they meet, for about 1½ inches, to merge into the labia majora They also contain sebaceous glands

The folds of the labia minora round the clitoris are known as the preputium clitoridis anteriorly and the frenum clitoridis posteriorly The clitoris corresponding to the penis, lies just below the anterior commissure or junction of the labia majora The triangle formed by the clitoris and the labia minora is known as the vestibule, and is furnished with small mucous glands on its surface. The urinary meatus lies in the vestibule an inch behind the clitoris

Behind this again is the vaginal introitus with the hymen or its remains, the carunculae hymenales

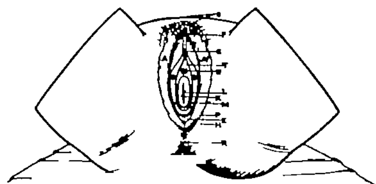


Fig. 7—The Female External Genitalia

A, labia majora *B*, labia minora *C*, clitoris *E*, frenulum labiorum ; *F* anterior commissure ; *H* posterior commissure *K* hymen ; *L*, vaginal orifice ; *M*, orifice of Bartholin's gland duct *P* vestibular fossa ; *R*, anus ; *S*, mons pubis ; *T* vestibule ; *U* orifice of urethra

and posterior fornices, this latter being the deeper and related to the pouch of Douglas. The cervix is pierced by a canal the ends of which are known as the external os and the internal os. The cervical canal is an inch long lined with columnar epithelium and furnished with numerous glands

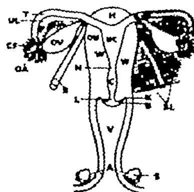


Fig. 9.—The Uterus and Appendages (Posterior View)

A, entrance to vagina, *B* Bartholin gland; *BL*, broad ligament *C*, cervix uteri; *CF* corpus fimbriatum *D* anterior lip of external os; *H* fundus uteri; *K* fornix *L*, external os uteri *N* internal os uteri *OA*, ostium abdominale *OU* ostium uterinum *OV* ovary *P* epoophoron *R*, round ligament *T* Fallopian tube; *UC*, cavity of uterus *UL*, ligament of ovary; *V* vagina; *W* body of uterus

The Uterus

The cavity of the uterus, which is continuous with the cervical canal at its internal os is lined by a columnar ciliated epithelium (Fig 9) There are many long deep glands with a similar lining The body of the uterus, which forms an angle with the cervix, is bent forward and lies on the bladder The broad ligament of peritoneum on either side divides to enfold the body of the uterus. At the upper end, or fundus of the cavity of the uterus on either side are the openings of the Fallopian tubes.

The Fallopian Tubes

The Fallopian tubes lie in the free upper borders of the broad ligaments and stretch from the uterus to the ovaries where they terminate in the fimbriated ends The outer ends of their canals are open to the peritoneal cavity The lining is of columnar epithelium. Below the Fallopian tubes and between the layers of the broad ligament lies cellular tissue which may be involved by an inflammatory process

EXAMINATION OF THE PATIENT

A careful history is taken including the present symptoms exposures to infection and past gynaecological ailments. Details of the menstrual history and all confinements or miscarriages

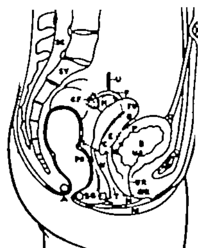


Fig 8.—General Anatomy of the Female Genito-Urinary System
A anus B bladder cavity BG, Bartholin gland and duct; C, cervix of uterus CF corpus fimbriatum D cavity of uterus E, body of uterus; F Fallopian tube FL fundus of uterus H ovary K anterior fornix L, posterior fornix LL 5th lumbar vertebra M labium majus; N labium minus OR, urethral orifice P vesico-uterine fold PD pouch of Douglas Q urachus R, rectum S symphysis pubis SC spinal canal; SI 1st sacral vertebra T vaginal orifice U ureter UA, orifice of ureter UR, urethra V vagina

Glands of Bartholin

These lie one on either side, encapsulated within the posterior third of the labia majora. The gland ducts which are lined by columnar epithelium, open on the inner sides of the lower ends of the labia minora on either side of the vaginal orifice.

The Urethra

This is $1\frac{1}{2}$ inches long perforates the triangular ligament and opens in the vestibule about an inch below the clitoris (Fig 8) At the mouth of the urethra, or just inside, are the two openings of Skene's tubules and there are also numerous gland follicles and lacunae along the length of the canal as in the male urethra, The urethra is lined with a columnar epithelium

The Vagina

The vagina curves downwards from the cervix uteri to the introitus at the vulva. The anterior wall is $3\frac{1}{2}$ inches long the posterior $4\frac{1}{2}$ inches long Its relations are anteriorly the bladder and urethra posteriorly the pouch of Douglas rectum and anal canal and perineal body and laterally the broad ligaments, ureters and levatores ani

Up to puberty the vagina is lined by a columnar epithelium, but in the adult this is altered to a stratified squamous epithelium

The Cervix Uteri

This projects into and is continuous with the vagina. The sulci formed by this projection are known as the anterior

be seen and a specimen of discharge may be taken for examination for *Trichomonas vaginalis* It is wise to make smear and culture examinations of specimens from the rectum.

The patient now lies flat on the couch. The inguinal glands are palpated and a bi manual examination is made to elicit the size and position of the uterus and to find out if there is any evidence of infection of the Fallopian tubes or of parametritis Finally a specimen of blood is taken for a Wassermann reaction and a complement fixation test

The smears are now stained and examined If gonococci are found, treatment may begin at once If results are negative, the patient must return in a few days when culture and blood test results are available. A provocative dose of 500 million organisms of a polyvalent gonococcal vaccine can be injected on the first visit if a positive result is not obtained and the tests repeated in forty-eight hours It is also sometimes of value to leave a tampon soaked in glycerine against the cervix for twenty-four hours before taking tests in chronic cases. If the case is suspect, tests must be repeated particularly after the menstrual periods for a minimum of three months.

ACUTE GONORRHOEA

In acute gonorrhoea the urethra the cervix, or both may be affected The symptoms bringing patients to seek advice may be pain or frequency of urination vaginal discharge, irritation or soreness of the vulva and thighs or occasionally swelling of the vulva due to an acute infection of a gland of Bartholin. The incubation period is usually as in the male, between two and eight days

An examination of a well-developed case may reveal a red and inflamed vulva with evidence of irritation of the upper thighs by discharge, a urinary meatus which is red and pouting and from which can be expressed pus, and a cervix discharging pus and possibly eroded round the external os If the Skene's tubules are infected, beads of pus may be seen at the duct orifices, and if a Bartholin gland is infected there may be a tender swelling in the lower end of the labium majus and the duct orifices will be inflamed and showing a bead of pus One or both Bartholin glands may be affected

In the acute case it is generally easy to find gonococci in

are obtained Great tact should be exercised in eliciting the history in order to put the patient at her ease

The history obtained varies with the stage of the disease. In acute gonorrhoea complaint may be of vaginal discharge, of troubles in urination of soreness of the vulva or vulval swelling In chronic cases the symptoms may be discharge, backache, abdominal pain or sterility Sometimes the first evidence of infection is an acute salpingitis.

Having taken the history a general examination of the patient is made, noting any lesions of the skin or mucous membranes and any glandular enlargement Local inspection now follows, for which the patient should be in the lithotomy position Vulvitis and any sign of irritation of the thighs and evidence of discharge may be seen The labia majora are separated and the vulva is swabbed clean with cotton-wool, dry or soaked in saline A close inspection is made for sores or ulcers. Discharge from vagina or urethra is noted and finally the glands of Bartholin are palpated between forefinger in vagina and thumb on the outer side of the lower end of the labium majus Next the forefinger is introduced into the vagina and the urethra massaged to bring any discharge to the meatus The patient should not have passed urine for two to three hours before this examination

A smear is made of the urethral discharge and a culture medium is inoculated If no discharge is visible the platinum loop is introduced into the urethra and drawn along the floor to collect a specimen. The lips of the meatus are now drawn apart and the orifices of the Skene's tubules examined If there is any discharge from the ducts of the glands of Bartholin, smears are made.

A vaginal speculum bivalve or Fergusson type, is now used to expose the cervix and any abnormalities such as erosion tears discharge etc are noted The cervix is cleaned with a cotton wool swab and a platinum loop is introduced well into the canal and the material so obtained is used to make a smear and to inoculate a culture medium If cultures are to be made no lubricant other than water is used on the speculum.

If any lesion of the cervix is suggestive of a syphilitic chancre a specimen of serum from its edge can be taken with a glass capillary tube for dark-ground examination As the speculum is withdrawn the condition of the vaginal wall can

be seen and a specimen of discharge may be taken for examination for *Trichomonas vaginalis* It is wise to make smear and culture examinations of specimens from the rectum

The patient now lies flat on the couch. The inguinal glands are palpated and a bi manual examination is made to elicit the size and position of the uterus and to find out if there is any evidence of infection of the Fallopian tubes or of parametritis. Finally a specimen of blood is taken for a Wassermann reaction and a complement fixation test.

The smears are now stained and examined. If gonococci are found, treatment may begin at once. If results are negative, the patient must return in a few days when culture and blood test results are available. A provocative dose of 500 million organisms of a polyvalent gonococcal vaccine can be injected on the first visit if a positive result is not obtained and the tests repeated in forty-eight hours. It is also sometimes of value to leave a tampon soaked in glycerine against the cervix for twenty-four hours before taking tests in chronic cases. If the case is suspect, tests must be repeated particularly after the menstrual periods for a minimum of three months.

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In the acute case it is generally easy to find gonococci in

smears taken from the urethra or cervix or both and from the duct orifice of an infected Bartholin gland

Treatment

As in the male, by far the best results will be obtained if the initial stages of the treatment can be carried out with the patient in bed Local treatment for the first week will be limited to baths and local hygiene If there is external irritation dusting powder calamine lotion or zinc cream can be used

Chemotherapy

Sulphapyridine for bed patients can be given in the same dosage as for the male namely 6 gm the first day and 4½ gm daily from the second to the fifth day — a total of 24 gm. For out patients 1 gm three times daily for seven days, a total of 21 gm., is as much as the average woman can take without showing signs of toxicity This is not really adequate dosage, and if sulphathiazole or sulphadiazine can be used so much the better Sulphathiazole and sulphadiazine may be given in doses of 6 gm daily for four days the doses being distributed as described in the treatment of gonorrhoea in men

Naturally fluid intake must be maintained on a high level and a light diet is chosen at the discretion of the patient.

A week after the start of treatment a second series of urethral and cervical smears and if possible cultures should be made during the course of a thorough examination By this time the average case will be nearly symptom free and all signs of acute infection should have markedly abated or disappeared If there is no pathological evidence of persistent gonococcal infection tests are repeated weekly for a month and if all are satisfactory the patient is ready for routine follow-up before tests for cure

A little thin vaginal discharge often persists for a short time after chemotherapy has ceased and a fortnight's treatment with Stovarsol as a routine in all cases is to be recommended

The patient should attend daily to have the vagina insufflated or dusted with Stovarsol powder after swabbing through a speculum If daily treatment is not possible two ¼ gm Stovarsol vaginal tablets can be inserted as high as possible into the vagina by the patient each night and morning

CASE RECORD VI ACUTE GONORRHOEA (FEMALE)

B. A. AGE 22 MARRIED (REFERRED BY HUSBAND)

History.—Marital coitus 7 days ago, two days before husband developed an acute gonorrhoea, contracted extramaritally. Complaining of slight dysuria and genital irritation. Slight discharge.

Examination.—Vulva red. Urethra exuding pus. Bartholin's glands normal. Cervix exuding thick muco-pus. No abnormality in pelvis.

Day	Urethra		Cervix		
	Smear	Culture	Smear	Culture	
1	G.C.+	G.C.+	G.C.+	G.C.+	Rectal smear and culture = no gonococci. Sulphadiazine, 6 gm. daily for 4 days. Bed. Hot baths. Dusting powder to vulva
7	G.C.–	G.C.	G.C.	G.C.–	Still some thin discharge from vagina. Daily application of Stovarsol powder to vagina. Twice-weekly application of glycerine and iodine to cervical canal
5–20					Menstrual period
8	G.C.	G.C.	G.C.	G.C.–	Stovarsol to vagina and treatment of cervix continued for one week
29	G.C.–		G.C.		Sign and symptom free
49	G.C.–	G.C.	G.C.	G.C.	After menstrual period
77	G.C.	G.C.	G.C.	G.C.	After menstrual period
03					Injection of 500 million organisms of polyvalent G.C. vaccine
105	G.C.	G.C.	G.C.	G.C.	Glycerine and gelatin pessary inserted on previous night. Pelvis — no abnormality. W.R. = negative. C.F.T. = negative
189	G.C.	G.C.	G.C.–	G.C.	No symptoms or signs. Blood tests repeated and remain negative. Discharged

Stovarsol has no effect on the gonococcus, but is a specific for *Trichomonas vaginalis* infection.

T. vaginalis is not uncommonly found as a secondary

infection with gonorrhoea in women and is a common cause of persistent vaginal discharge after a gonorrhoea has been cured Whether *T vaginalis* is found or not Stovarsol has always an excellent local drying action. The diagnosis and treatment of *T vaginalis* are discussed in detail on page 320.

During the two-week period of local treatment it is a good plan twice a week to treat the cervical canal with equal parts of glycerine and tincture of iodine introduced by means of a Playfair's probe dressed with cotton wool, which can be insinuated through the external os along the whole length of the canal and gently turned round once or twice when *in situ* The vast majority of early acute gonorrhoeas will need no more treatment than this

If at any time gonococci are found during tests, a careful search is made for any obvious focus of infection The urethra, Skene's tubules and the urethral glands are likely places and persistent infection deep in the glands of the cervix is not uncommon Treatment of clinical or pathological relapse cases will be by chemotherapy with a different sulphonamide from that first used and local treatment as will be described under various anatomical headings

Sulphonamide resistance, apart from any complications, is not infrequent. In such cases, as in the male a change of drug alone or in conjunction with fever therapy is very often successful. In repeating courses of sulphonamides, a lapse of from seven to ten days should be allowed between courses, and before a third course of chemotherapy a red and differential white blood cell count will be necessary

URETHRITIS

Acute urethritis is characterized by pain and frequency of urination and by a discharge of pus from the urinary meatus The majority of cases are cured by chemotherapy without local treatment Persistence of gonococci in the urethra may be due to infection of a urethral gland or glands

Diagnosis of this condition can sometimes be made by palpating the urethra through the vaginal wall over a straight metal sound when the infected glands may be felt as hard and sometimes tender nodules varying in size from a grape seed to an orange pip Massage of the urethra against the

sound is sometimes followed by a discharge of pus when the sound is removed. Treatment in such cases, apart from coincident chemotherapy consists of massage of the urethra over a sound once or twice weekly followed by a lavage of the urethra with a 1 10,000 solution of potassium permanganate and then instillation of glycerine into the urethra by means of a rubber catheter on a syringe. Irrigation of the urethra can best be done with a douche-can by the gravity method and a Janet nozzle is quite effective. The bladder can be filled up in the same way as in posterior irrigation for the male.

Examination of the urine can be used in assessing progress, but is not a very satisfactory test as a certain amount of mucus is very often present in the urine of a healthy woman The only thorough way is by frequent examination of smears and cultures and treatment may cease when four weekly negative tests have been returned The patient should not urinate for at least two hours before tests, and it is as well to make the tests after the urethra has been massaged over a sound so that the expressed contents of the glands can be disclosed.

Infections of Skene's tubules are not uncommonly the cause of a persistence of urethritis or of relapse. The orifices at, or within, the meatus are red and elevated in infection and pus can be made to exude on squeezing or after massage of the urethra over a sound

Skenitis should be treated by cauterising the lengths of the ducts with electrocautery under general anaesthesia with Evipan or Pentothal.

UPPER URINARY TRACT

The diagnosis and treatment of the rare cases of gonococcal cystitis, pyelitis or pyelo-nephritis occurring in the female are the same as have already been described for the male

VULVITIS

In some cases of acute gonorrhoea, where there is a profuse discharge of pus from the urethra or vagina, the vulva and upper thighs become inflamed and the patient complains of irritation and soreness The vulva is red and there is often

peeling of the epithelium, sometimes with actual ulceration. On rare occasions it is possible to isolate the gonococcus in smears or cultures taken from such ulcers

Vulvitis resolves very rapidly as the general infection comes under control by chemotherapy and the local irritation is soothed by the application of talcum powder of calamine lotion containing 2 per cent phenol, or of a zinc cream Rest and *frequent hot baths complete the treatment.*

INFECTION OF BARTHOLIN'S GLANDS (ACUTE BARTHOLINITIS)

In acute gonorrhoea it is not uncommon to find evidence of infection of one or both glands of Bartholin or of their ducts. Cases coming early under observation usually show only a redness of the duct orifices possibly with a small exuding bead of pus in which gonococci can be found Less often in an early case, an established Bartholinitis or a gland abscess may be the reason for the patient's seeking advice

An acutely inflamed gland can be felt as a hard tender lump in the lower end of the labium majus. One or both sides may be affected and some vulval swelling is usual although less in such cases than when the condition has progressed as far as abscess formation With abscess formation there is great oedema swelling and redness of the vulva on the affected side and fluctuation can be felt over the abscess cavity

The patient with acute Bartholinitis or abscess complains of severe pain increased in walking and of the swelling of the vulva *The complement fixation test is positive often strongly* positive in a high percentage of cases of acute Bartholinitis or abscess

Treatment

The earliest cases, where the condition has not progressed as far as abscess formation can generally be cured by chemotherapy combined with local treatment of frequent hot baths and fomentations A patient should of course be confined to bed

If an abscess forms it should be widely opened under general anaesthesia, the incision running antero-posteriorly through the labium majus The cavity should be packed daily with

CASE RECORD VII BARTHOLINITIS AND SKENITIS

D C. AGE 28. SINGLE

History—Exposed t infection 3 weeks ago. Slight vaginal discharge for 2 weeks. Swelling of vulva for 2 days.
Examination—Vulva red. Hard tender swelling of Bartholin gland in left labium majus. Duct orifice red and exuding pus. Pus expressed from urethra. Cervix normal, with clear mucus t os. No abnormality in pelvis.

Day	
	Gonococci in smears and culture from urethra and left Bartholin's duct. N gonococci from cervix. C.F T = strongly positive. Sulphadiazine 6 gm. daily for 4 days. Bed, hot baths, and hot fomentations to vulva
4	Swelling now fluctuant. Widely opened under Pentothal anaesthesia. Wound packed with sulphanilamide powder Ribbon gauze drain
5–13	Daily hot bath and re-dressing Wound granulating slowly
14	No gonococci in smears or cultures from urethra, cervix and abscess cavity
16–21	Menstrual period
23	Healed. Full tests. Gonococci found in urethral smear Skene's ducts inflamed and exuding little pus. Ducts deeply cauterized with electrocautery under Pentothal anaesthesia
24–27	Sulphathiazole 6 gm. daily for four days. Frequent hot baths
34	Full tests. No gonococci in smears or cultures
8 72, 107	Full tests after menstrual periods. No gonococci found. No symptoms or signs
35	Full tests after menstrual period. No gonococcus found. W.R. and C.P T both negative. N symptoms or signs
[illegible] 9	All tests repeated and negative. Discharged cured

ribbon gauze during the period of healing and allowed to granulate up. The treatment of election of earlier days with a complete removal by dissection of the affected gland and duct is now an unnecessary elaboration When a Bartholin s abscess has ruptured before treatment is sought, it is best to proceed in a like manner by increasing the opening laying bare the cavity and opening up any fistulous tracks.

SUBACUTE AND CHRONIC BARTHOLINITIS

Such cases may follow an acute infection or may be indolent from the start and only discovered on routine examination. Symptoms and signs are less than in the acute infections but are liable to be most obvious at the times of the menstrual periods. There may be some slight swelling of the labium majus on the affected side and the duct orifice is generally obvious, red and wider than normal Palpation reveals the affected gland as a hard sometimes fibrous, tender mass, and massage may produce a little discharge of pus from the duct

Gonococci may be seen in or cultured from, this expressed pus Diagnosis is often helped in suspect cases, when gonococci cannot be isolated by the complement fixation test which is positive in a high percentage of instances A cyst sometimes follows an untreated abscess or results from obstruction of the duct in an originally subacute or chronic infection

Treatment

If the infection is not too long established many cases will yield to chemotherapy and local application of heat A few will be stimulated to activity by local treatment go on to abscess formation and require opening The most chronic with fibrosis of the gland or cyst formation are best treated by a complete removal of the gland by dissection The cavity should be allowed to granulate up from the bottom if it is suspected that the gland has not been removed entire.

VAGINITIS

Gonococcal infection of the vaginal wall is rare in adults and when it does occur is usually associated with pregnancy In a true gonococcal infection the organism can be isolated from material taken from the vaginal wall and the most likely place for an infection is in the fornices near the cervix In an acute gonorrhoea with profuse cervical discharge the vagina may become oedematous appear red and granular and bleed when the speculum is passed for inspection Chemotherapy followed by Stovarsol insufflation or vaginal tablets

rapidly cures most cases whether truly gonococcal or the commoner secondary irritative variety

Insufflation may be preceded in the worst cases by a gravity vaginal douche with a solution of sodium bicarbonate, a drachm to the pint, to clear away the discharge.

If the condition persists in spite of such treatment, the most likely cause is a *Trichomonas vaginalis* infection, the investigation and treatment of which is considered elsewhere.

THE CERVIX

Infection of the cervix is usual but not invariable in acute gonorrhoea. Chronic infection is common, and the cervix can be regarded as a counterpart of the prostate gland in the male, an excellent hiding place for gonococci, with innumerable tortuous glands difficult of access for treatment.

ACUTE CERVICITIS

Symptoms are usually slight although there may be some complaint of backache or lower abdominal pain. The amount and quality of the discharge varies from profuse purulent to a watery or mucoid leucorrhoea. The urethritis which usually accompanies cervicitis is more likely to be the producer of symptoms which bring the patient to seek advice

On examination, the vagina is usually seen to contain pus or an excess of mucus From the cervical canal exudes a discharge, purulent blood-stained muco-purulent or watery It is impossible to tell from the aspect of the exudate whether the infection is gonococcal or not

The cervix, after being swabbed clean, may show some signs of erosion round the os Erosion is commonest in multipara but is often found in nullipara. Gonococci can easily be isolated by smear or culture in acute cases

Treatment

Whether the cervix is eroded or not, early acute cases resolve quickly on chemotherapy with a minimum of local treatment As already described the cervical canal can be medicated twice weekly during the early stages with a mixture of equal parts of glycerine and tincture of iodine

When the complement fixation test is positive originally its return to negative is a sign of great value in assessing progress.

Sulphonamide therapy will be employed in the preliminary stages and if necessary repeated later with a change of drug The use of T.A.B fever combined with chemotherapy should not be forgotten in resistant cases.

Sometimes a case is encountered where gonococci can easily be recovered from the cervix but where the complement fixation test is negative and chemotherapy and local treatment cannot produce a cure. In such a case as indeed in any chronic cervicitis vaccine therapy is of the utmost value. A course consists of ten injections, starting with ½ c.c. ½ c.c., then the maximum dose of 1 c.c. up to the tenth injection using a polyvalent gonococcal vaccine containing 500 million organisms per c.c. Injections are given every other day After such a course a negative complement fixation test will generally have changed to positive, and sulphonamide therapy may be effective where it has previously failed

UPPER GENITAL TRACT : THE UTERUS

Clinical endometritis or metritis is very uncommon although an infection must certainly be present to some extent in cases which have a salpingitis, and sometimes may be masked by signs of the latter condition. When infection of the endometrium occurs, it usually follows childbirth or abortion

In acute endometritis the patient has generally a history of vaginal discharge and complains of lower abdominal pain and backache The temperature is raised sometimes as high as 104 F The uterus is tender and bulky on bi manual examination. A history of gonorrhoea or the finding of gonococci with a recent childbirth or abortion will help in the diagnosis

Treatment consists of rest in bed in the Fowler position to assist drainage hot applications to the abdomen and the administration of a sulphonamide, preferably sulphathiazole or sulphadiazine After a day or two when acute symptoms have subsided gravity vaginal douches using four to six pints of hot (110 F) potassium permanganate 1/10 000 solution can be given Glycerine and gelatine pessaries should be used nightly to promote drainage and when the acute phase has

passed, local treatment to the cervix as already described will usually be necessary

If later a chronic infection is suspected the cervix should be dilated under anaesthesia and a rubber catheter inserted in the uterine cavity and stitched to the cervix. For a few days until the stitch breaks loose, glycerine is injected through the catheter into the uterus Further sulphonamide therapy follows this treatment, and the results are most satisfactory

THE FALLOPIAN TUBES

Salpingitis is the most important of the local complications of gonorrhoea in women The infection may be coincident with, or follow shortly after an acute gonorrhoea or it may be an isolated event in a case where the original infection has passed unnoticed. The findings in patients operated in acute attacks vary from a mild inflammatory reaction in and around the affected tube to a pyo-salpinx. Symptoms of salpingitis usually coincide with a menstrual period or follow childbirth or abortion

ACUTE SALPINGITIS

An acute salpingitis is characterized by general malaise, vomiting, a raised temperature and pulse rate, and abdominal pain The pain is felt in the lower abdomen and back and may radiate to the vulva. It is often intermittent, sudden colicky pains being superimposed on a general dull ache, and if the right side is affected, may cause confusion in diagnosis with appendicitis Seldom however is the general condition of the patient so bad as that found in acute appendicitis Other conditions to be considered in differential diagnosis are tubal pregnancy and twisted ovarian cyst.

On examination signs may be found of acute or subacute gonorrhoea, and if it is possible to make pathological tests, the gonococcus may be demonstrable. The complement fixation test is usually positive but naturally is not of much help in making an urgent diagnosis. The abdomen is generally tender but signs are most apparent on one or other side and there is rigidity of the overlying muscles. There is usually also some hyperaesthesia of the skin of the abdomen over the

affected tube A bi manual examination which should invariably be done in any case of pelvic pain in women will reveal tenderness and possibly a mass palpable in the pelvis on one or other side Salpingitis is often accompanied by a certain amount of parametritis, inflammation in the connective tissue of the broad ligament and sometimes by pelvic peritonitis.

CASE RECORD VIII SALPINGITIS AND PARAMETRITIS

F E. Age 35 Married 5 Children

History—For 5 months, continuous backache and lower abdominal pain. During menstrual periods the abdominal pain becomes severe and colicky and she must rest in bed. Has had slight clear vaginal discharge for 2 years since birth of last child. Has just finished menstrual period when pain was very severe but has now abated.

Examination.—Temperature 99 F., pulse 80. General abdominal tenderness to touch, most pronounced in left iliac fossa. Muscular rigidity in same area. Bi-manual examination — tender in both sides of pelvis, and small mass is palpable on left side. Only other abnormality cervical erosion. No gonococci in urethral or cervical smears. Admitted to hospital.

Day	
1 7	Bed, hot baths, hot douches, and Antiphlogistine poultices to lower abdomen. Sulphathiazole 6 gm. daily for 4 days. No gonococci grown from cultures taken from cervix and urethra on first day but complement fixation test returned strongly positive Husband seen and admits [illegible] gonorrhoea one year ago
8	Symptoms markedly subsided. Pelvic mass still palpable Temperature normal for 5 days. Under Pentothal anaesthesia cervix fully dilated and rubber catheter left in uterus stitched to cervix with silkworm gut. Sterile glycerine injected through catheter three times daily for five days until catheter came loose
7	Discharged hospital. Pain and backache gone To rest until after next period
50	Full tests. Gonococci present in cervical culture C.F.T. [illegible] positive No symptoms since leaving hospital. Cervical erosion cauterized with cautery Sulphadiazine 6 gm. daily for 4 days. Cervical canal treated twice weekly with glycerine and iodine
58	Full tests No gonococci [illegible] in smears or cultures. C.F.T. weakly positive No symptoms Erosion healed. Pelvis appears normal. Treatment of cervix continued for three weeks
86–98	Full tests after menstrual periods. No gonococci found. No symptoms or signs C.F.T. permanently negative
162	All tests, including W.R. negative [illegible] Free of symptoms. Pelvis normal Discharged

If such is the case the findings by bi-manual examination are more positive General peritonitis occurs but rarely

If a positive diagnosis of acute salpingitis can be made, treatment should be conservative, but if any doubt exists, a laparotomy should be done to establish the diagnosis

Treatment

The patient is confined to bed in Fowler's position, and will remain there until all symptoms have subsided and until the temperature and pulse rate have been normal for a week. If no sulphonamides have been given or none recently a course is indicated and sulphathiazole or sulphadiazine will be used for preference, being least likely to cause upset. Hot applications are applied to the lower abdomen and morphia may be necessary once or twice in the early stages

After a few days, as the symptoms subside, gravity douches with potassium permanganate (1 10 000 solution at 110 F) can begin and glycerine and gelatine pessaries are used each night The case must be well watched, for although most will subside rapidly there is always the possibility of a peritonitis and laparotomy must be performed if signs of general abdominal rigidity with a rising pulse-rate should appear

Pelvic abscess is also a possibility and is characterized by a persistence of pain swinging temperature and a pelvic mass which may bulge into the pouch of Douglas Here operative interference will be necessary either by the vaginal or abdominal route, at the discretion of the surgeon

In the majority of cases, however surgery can and should be avoided When the acute stage has abated, local treatment of the cervix begins and the case is watched and tested over a long period. The results of complement fixation tests are of great assistance in assessing progress The end result may be a functioning tube, but not infrequently some chronic infection remains and will require further treatment.

SUBACUTE AND CHRONIC SALPINGITIS

A low-grade inflammation not infrequently follows acute salpingitis, or the condition may be chronic from the start. Chronic salpingitis is characterized by general ill health, back ache and abdominal pain and possibly vaginal discharge. The

pain is worst at the menstrual periods and there may be some disturbance of the menstrual cycle with dysmenorrhoea and menorrhagia Bi manual examination generally reveals some thickening of the pelvic tissues on one or other or both sides and sometimes a definite mass when a chronic pyo- or hydrosalpinx is present Attacks of subacute or acute salpingitis are often superimposed on the chronic condition The complement fixation test is usually positive and is a great help in diagnosis in such cases when the gonococcus cannot be isolated from cervix or urethra.

Treatment

A certain number of chronic cases may be cured or at least alleviated by the minor procedure of dilatation of the cervix, stitching in a catheter and injecting glycerine as already described this procedure being followed by chemotherapy and local treatment:

If however no relief is obtained or if there is evidence of persistence of infection as shown by a fixed positive complement fixation test it may be necessary to consider salpingectomy The results of this operation in picked cases are very good but all aspects of the case must be considered and other methods tried before it is advised particularly in women where future child bearing is a consideration

FOLLOW-UP AND TEST OF CURE

When the patient is free of signs and symptoms and when *all active treatment has ceased* a period of *observation begins*. The patient should attend immediately after the cessation of the menstrual period for three consecutive months for investigation including a bi manual examination and pathological tests

Urethral and cervical smears and cultures are examined and tests are made also from the rectum if this has been originally involved Cultural examinations are very important and should be done whenever possible and certainly on the third occasion Alcohol may be resumed after the first test if this is negative A provocative injection of 500 million organisms of a polyvalent gonoccocal vaccine should be given 48 *hours before* the third test *Blood* is taken also at the third test for the complement fixation test and

Wassermann reaction. If all tests are negative, the patient should be seen again in three months if possible, and again after a menstrual period when vaccine provocation and all tests including the complement fixation test are repeated If all the preceding tests are negative the patient may be pronounced cured

The finding of gonococci at any test will necessitate a search for the focus of infection and its local treatment combined with further chemotherapy If the complement fixation test is found positive and is positive on repetition in the absence of any known past complication, the pelvic organs, Bartholin s glands and the cervix will be most suspect. A positive complement fixation test after a complication will cause alarm only if it does not decrease and become negative with the passage of time

In marital cases when both partners are infected, it is most important to ensure a complete cure of both man and wife before they are permitted to resume sexual intercourse otherwise reinfection and reactivation takes place, aptly called gonotennis by French authors

GONORRHOEA AND PREGNANCY

Gonorrhoea is not markedly different in pregnant women The signs and symptoms are the same but there is usually more discomfort from vulvitis and irritation of the thighs, as vaginal discharge tends to be more profuse Vaginitis, when it occurs, is likeliest in pregnancy

In the puerperium sepsis may be caused by the gonococcus alone or in conjunction with other organisms or salpingitis and parametritis may occur rather later

Treatment

Gonorrhoea in pregnancy is treated on the same general lines as for the non pregnant woman The sulphonamides are usually well tolerated but it is best to use sulphathiazole or sulphadiazine if possible, since they are least likely to cause upset. In dealing with the cervix, the greatest care should be taken to avoid trauma in treating the cervical canal. Follow-up tests are continued right up to term and tests of cure should not be done until a month or two after delivery Even in apparently cured cases, a most careful watch should be kept on the infant s eyes for a week or two after birth

Chapter V

ASPECTS OF GONORRHOEA COMMON TO BOTH SEXES

CHRONIC GONORRHOEA

Chronic gonorrhoea is as rare in the male as it is common in the female. A gonococcal infection should be called chronic, says Dr Jules Janet, if when left untreated at no matter *what stage of the disease, it does not relapse into a clinical* state of acute or subacute gonorrhoea This definition excludes the difficult and resistant cases in both sexes where if treatment is suspended the original signs and symptoms quickly reappear

Gonorrhoea may persist as a chronic state for many years after infection particularly in women but there is a strong natural tendency to spontaneous cure.

A The Male

In the male the urethra is acutely inflamed in early *gonorrhoea, but a true chronic infection of the urethral* mucosa is excessively rare. The gonococcus in chronic gonorrhoea is to be found in some extra urethral structure, such as a Littré s or Cowper's gland the prostate or seminal vesicles or a para urethral duct Gonococci must from time to time traverse the urethra in such cases but without reactiva tion no a ute urethritis develops Unlike the female it is rare for the male to develop a chronic state of gonococcal infection without a very obvious and unmistakable acute stage.

The male carrier of gonococci often has little to show clinically There may be a slight gleet or morning discharge with the urine showing some threads or debris On the other hand the infection may only be suspected if a partner is infected or if some provocation such as a bout of alcohol or sexual activity reactivates the organism and all the signs of acute gonorrhoea reappear Again iritis or rheumatism may be instrumental in causing a search for the gonococcus It should be remembered that it is not impossible for a person with chronic gonorrhoea to acquire a super infection pro-

ducing an acute urethritis. The fact that the gonococcus is showing little or no sign of activity in one host does not mean that its virulence is lost. Passed to another it is restored to vitality and produces an acute gonorrhoea.

In suspected cases repeated examinations are necessary over a long period Exact diagnosis is often difficult and culture and serological tests must be included. Provocation by means of alcohol gonococcus vaccine and instrumentation of the urethra is used to reactivate any gonococci in concealed foci of infection and to make their discovery easier in pathological tests.

Treatment is directed at the focus of infection when it is discovered and fever therapy has an important role in chronic gonorrhoea in conjunction, of course, with a sulphonamide

B The Female

Chronic gonorrhoea in the female is very common indeed and is responsible for much spread of the disease. Symptoms may be very slight and are often absent entirely Skene's ducts the glands of Bartholin, the cervix and Fallopian tubes are all foci which may harbour the gonococcus. A persistent vaginal discharge, an attack of salpingitis, a metastatic complication or the infection of a partner may bring the patient to seek advice.

Diagnosis is no easier than in the male and examinations and complete pathological tests must be carried on over a period of months in some cases before the gonococcus can be isolated Tests should be done immediately after the menstrual periods as well as at other times and provocation by vaccine and application of glycerine to the cervix is used. Local treatment is aimed at the focus of infection, with fever and sulphonamide therapy for general effect.

GONORRHOEA AND MARRIAGE

A patient male or female who has been treated and tested for cure on the lines indicated in previous chapters, may without reservations be allowed to marry If, however a patient, having had a gonorrhoea in the past and unsatisfied that tests of cure were adequate, requests an opinion as to fitness for marriage, a comprehensive series of tests must be undertaken before a confident answer can be given

In the female, there must be no physical signs, the complement fixation test must be negative, and urethral and cervical smears and cultures after provocation and after menstrual periods for three months must reveal no gonococci

For men there must be no physical signs of disease, the complement fixation test must be negative and smear and culture examinations of intra-urethral and prostatic specimens on four weekly occasions must disclose no gonococci. Provocative measures should also form part of the test

Coitus is likely to reveal infection where the foregoing tests have been negative and a man can be recommended to use a condom for a month or two after marriage. In the early days of marriage this is not likely to make his wife suspicious.

GONORRHOEAL AFFECTIONS OF THE EYE OPHTHALMIA NEONATORUM

Infection of the conjunctiva of the infant during the process of birth is a fairly common occurrence Such an infection usually becomes apparent within forty-eight hours of birth and cases occurring after a longer interval can often be traced to a later contamination by an infected person

When conjunctivitis is present at birth an upward spread of infection after the rupture of the membranes has occurred

The gonococcus is the most important cause of ophthalmia neonatorum and can be avoided only by the careful treatment and observation of infected pregnant women and by the prophylactic treatment of the eyes of infants immediately after birth. The common practice of instilling into the infant's eyes a few drops of 1 per cent silver nitrate solution or of 10 per cent silver proteinate solution is satisfactory If silver nitrate is used the excess should be neutralized with salt solution after a few minutes to avoid a chemical conjunctivitis

The diagnosis is made by finding the gonococcus in smears of pus taken from the infected conjunctival sac One or both eyes may be affected and the clinical picture is of swelling and oedema of the lids a free discharge of pus and matting together of the lashes with exudate The conjunctiva is red and granular and there may be corneal ulceration If treatment is neglected, spread of infection may go so far as to

produce panophthalmitis These cases should always be treated in hospital Ophthalmia neonatorum is a notifiable disease and the medical officer of health will arrange disposal of cases.

If only one eye is affected it is important to avoid contamination of the healthy eye This is achieved by washing the healthy eye carefully with normal saline or a 1 per cent boric acid solution from a large undine, instilling 10 per cent silver proteinate solution, and covering the eye with a pad of cotton wool or sealing a watch glass over it with adhesive tape. The healthy eye is carefully examined each day

Excellent results are now obtained with combined sulphonamide and local treatment Sulphapyridine appears to be slightly more effective than sulphadiazine or sulphathiazole For infants an initial dose of ¼ gm. should be followed by ⅛ gm. six hourly for five days The dose is crushed up suspended in water and given in a feeding bottle.

Local treatment consists in four-hourly irrigations of the conjunctival sac with normal saline or 1 per cent boric acid followed by instillation of 10 per cent silver proteinate solution Atropine solution ½–1 per cent, can be instilled once or twice daily if there is any haziness of the cornea. The local condition clears up in forty-eight hours in most cases and gonococci rapidly disappear from the secretions. After the acute condition has subsided instillation of 4 per cent zinc sulphate solution four times daily for a few days may be necessary The use of sulphonamide powders, solutions or ointments for such cases has been tried but they are not nearly so effective as oral administration. For complications such as corneal ulcer or deep infections of the eye a specialist ophthalmic surgeon must be consulted at once

The results in cases coming early under treatment are good and vision is usually unimpaired but scarring of the cornea and blindness may follow ulceration of the cornea and deep infections

GONORRHOEAL CONJUNCTIVITIS IN THE ADULT

Adults or children with vulvovaginitis, may contaminate their eyes directly by the fingers or by contact with infected towels or other articles they handle The strictest instructions

must be given to all patients with gonorrhoea about washing their hands after touching the genitals and about keeping face and body towels separate. Chance infection of a healthy person's eyes by contaminated towels is possible and it is a general experience that such cases are always very severe and often lead to blindness. This may be because there is no developed immunity such as is present in a person who has already had a genito-urinary infection before the eye condition appeared. Treatment of the affected and unaffected eye is essentially the same as in the child. Sulphonamides are given in the same dosage as is recommended for acute gonorrhoea.

A meningococcal conjunctivitis is not uncommon and presents a clinical picture indistinguishable from that caused by the gonococcus. In such cases however there is no genito-urinary infection and the diagnosis will be made from the characteristics of the organism on culture. The condition is generally less severe than a gonococcal infection but the treatment is the same.

METASTATIC AFFECTIONS OF THE EYE

A Conjunctivitis

A mild conjunctivitis is sometimes seen with acute or subacute gonorrhoea and also in association with metastatic complications such as arthritis. Metastatic conjunctivitis is always bilateral. The conjunctiva is red, but there is little or no pus formation and gonococci are not found in secretions. The condition is transitory and resolves readily under sulphonamide treatment combined with local irrigation with 1 per cent boric acid solution. A careful watch should be kept for this is sometimes a forerunner of iritis.

B Iritis and Irido-Cyclitis

A true iritis with irregularity of the pupil and circumcorneal redness is not uncommon with the severe metastatic complications particularly polyarthritis. The condition may be unilateral or bilateral. Iritis also occurs quite apart from any other metastatic phenomena in chronic untreated or uncured gonorrhoea sometimes after a considerable lapse of time from the acute symptoms. Such cases present difficulties in diagnosis, but the complement fixation test gives an indication as to

whether a complete genito-urinary investigation is necessary A Wassermann reaction is also done at the same time, as syphilis is a possible cause of iritis.

An iritis case is often flared up if a fresh gonorrhoea is contracted after cure. The signs are those of any acute iritis with conjunctival redness irregularity of the pupil the patient complaining of headache and pain in the eye. In the worst cases there is sometimes haziness in the anterior chamber and vision is much impaired

Treatment

The source of infection must be found and eradicated In the male, the prostate and vesicles, and in the female, the cervix, Fallopian tubes and Bartholin s glands, are the first suspects in the investigation General treatment will consist of a course of a sulphonamide combined with T.A.B fever therapy if the general condition of the patient is good This is followed by a series of injections of polyvalent gonococcal vaccine containing 500 million organisms per c.c. The first injection should be 0·1 c.c. to avoid possibility of a flare-up Subsequently injections can be given every other day in rising dosage to a maximum of 1 c c The course will consist of twelve injections

Locally the iris is kept dilated with atropine drops (4 grains to the ounce) or with 1 per cent atropine ointment to avoid adhesions, and hot pads are applied to relieve the pain in the acute stages A shade is worn. With energetic treatment a good result can be obtained in most cases It is wise to have the co-operation of an ophthalmic surgeon in treating any such cases

GONOCOCCAL PROCTITIS

Infection of the rectum in male perverts is sometimes found and the male rectum may also be contaminated by the rupture of a prostatic abscess In women and children the rectum is not infrequently contaminated by the vaginal discharge, but symptoms are slight and the disease is often only recognized when pathological tests, taken as a routine, are returned positive.

There is usually very little discharge, but patients may complain of an excess of mucus at or after defaecation and of

anal irritation and pain. Signs of disease are slight but a proctoscopic examination may disclose some reddening of the rectal mucosa and in neglected cases even ulceration, and the mucosa bleeds easily

The condition yields rapidly to a routine course of a sulphonamide Local treatment if necessary can consist of daily rectal irrigations with a 1/10,000 solution of potassium permanganate and simple rectal suppositories

GONOCOCCAL STOMATITIS

This condition has been described in the new born and in such cases is contracted during the birth process in the same way as an ophthalmia A few cases occurring in adults have been described in the past There is said to be redness and ulceration of the buccal mucous membrane with bleeding from the gums A case has also been described where a nurse treating an infant with gonorrhoea, contracted a gonococcal infection superimposed on an existing stomatitis of different origin

Urethral gonorrhoea contracted by buccal coitus is described by Janet, who considers it to be simply a transference of infection from one client to another because the cases occurred in frequenters of a brothel A metastatic stomatitis has also been mentioned as occurring in gonorrhoea

GONOCOCCAL AFFECTIONS OF THE NERVOUS SYSTEM

Peripheral neuritis is a very rare complication of gonorrhoea the focus of infection generally lying in the male in the prostate gland at which efforts in treatment should be directed Myelitis and meningitis of gonococcal origin have also been described Recently a case of gonococcal meningitis which recovered after sulphanilamide has been recorded

GONOCOCCAL SEPTICAEMIA AND ENDOCARDITIS

Blood borne infections occur usually in association with an abscess in the prostate in the male or in a Fallopian tube in the female, but can be found with apparently straightforward uncomplicated acute cases and in children with vulvovaginitis or ophthalmia. Women appear to be affected oftener than men

The symptoms are the same as in any other septicaemia with swinging temperature, wasting anorexia and so on Purpuric rashes or even cutaneous abscesses may be seen Changes in the heart sounds due to vegetations on the valves are common.

Gonococci can often be cultured from the blood, during life, in such cases and are found easily in smears made post mortem from valvular vegetations Gonococcal septicaemia was almost invariably fatal in pre-sulphonamide days, but the prognosis is now better Gonococcal bacteraemia is probably commoner than is suspected in cases of severe polyarticular arthritis

GONOCOCCAL AFFECTIONS OF THE SKIN

Cutaneous abscesses on or near the genitals from which the gonococcus can be isolated are sometimes found with a gonorrhoea in either sex. A woman seen recently had a superficial ulceration of the inner side of the right thigh from which gonococci were cultured and no evidence of gonorrhoea could be found in the urogenital tract. Cases of multiple metastatic cutaneous abscesses containing gonococci have been seen on rare occasions

Skin eruptions are rare in gonorrhoea. They have been classified by Buschke as follows (1) simple erythema, occurring in acute cases, and to be distinguished from drug eruptions (2) urticaria and papular erythema sometimes encountered with gonorrhoeal arthritis (3) purpuric and bullous eruptions of embolic origin (4) hyperkeratosis.

The last is the only one likely to be encountered. The eruption is found in association with the most severe cases of metastatic gonorrhoea, particularly arthritis, and is known as keratoderma blennorrhagica. The condition usually occurs on the soles of the feet, but sometimes extends to the legs, palms of the hands and the body The original lesion is a small vesicle with a thick white areola and such vesicles are often seen alongside the fully developed crusts. The terminal lesions are dry heaped-up rupial masses of epithelium when fully developed A circinate balanitis resistant to treatment commonly found in association with arthritis, with or without other skin lesions, is considered by some authors to be a mani-



Fig 10.—Keratoderma Blennorrhagica
Below more advanced

festation of keratoderma blennorrhagica (Fig 10) In cases of keratoderma blennorrhagica of the feet the sufferers are usually men whose occupations entail a great deal of standing or walking for example, policemen

The condition has to be differentiated from psoriasis and rupial syphilides The history presence of arthritis and evidence of genito-urinary infection will generally be sufficient The Wassermann reaction and complement fixation test will tell more, and the psoriatic will usually have lesions elsewhere and the crusts are less mountainous and easily removed

Treatment

Local application of a 2 per cent salicylic acid ointment combined with general treatment of the focus of infection removes the condition without difficulty

GONORRHOEAL RHEUMATISM

This heading covers a number of allied conditions, including arthritis, synovitis periarthritis tenosynovitis, fasciitis bursitis myositis and periostitis One joint may be affected but usually there is a polyarthritis, and males are affected oftener than females Affection of the structures surrounding joints is on the whole commoner and certainly more obvious than a true arthritis and synovitis. *The condition is due to a* gonococcal toxin emanating from an undrained focus of

infection, although the gonococcus has on rare occasions been isolated from synovial fluid and from joint structures in such cases. Suppuration in gonococcal arthritis is very uncommon The rheumatic affections rarely coincide with acute urethritis except when a case has previously been a subject of metastatic complications It can arise from a few weeks to months or even years after the original infection

When a case is diagnosed, it is essential to locate the focus of infection, which in the male is likeliest to be in the prostate, vesicles or Littré's glands, and in the female, in the Fallopian tubes, Bartholin's glands or cervix. The complement fixation test is a very good guide as it is positive in about 90 per cent of true cases. Smear and culture tests will also be used on specimens taken from the usual sites

The parts usually affected are, in order of frequency knees, ankles, plantar fascia, wrists hands and feet, back, sternoclavicular and temporo-mandibular joints and shoulders. Periostitis is rare and coincides with arthritis or fasciitis. The calcaneus, tibia and ulna are possible sites, and bony spurs may be formed at the points of insertion of tendons or fasciae. Myositis is uncommon, but may occur in the muscles concerned with an affected joint.

Gonorrhoeal rheumatism may be acute or chronic. Rheumatism in one attack of gonorrhoea usually means that it will occur again in subsequent attacks, often in a severer form. In association with severe arthritis other metastatic phenomena often occur These include conjunctivitis, iritis, keratoderma blennorrhagica and very rarely urticaria or papular erythematous rashes

Clinical Types

Acute Local Affections The commonest type of acute affection is that of one or more large joints, the knees being oftenest involved. The first signs are of pain and stiffness about the joints, with redness and swelling later The swelling may be mainly periarticular but there is usually a varying amount of fluid in the joint cavity and sometimes synovitis is the main feature. The joint is tender to touch particularly near the tendinous insertions of the muscles. There is often some fever This type usually occurs with an attack of gonorrhoea or within a short time of an apparent cure, so that diagnosis, clinical and

pathological should not present many difficulties The complement fixation test will help if there is any doubt

If facilities are available, there is no doubt that hypertherm treatment for such cases gives the best and quickest results. In the absence of hypertherm) the patient should be treated with rest in bed heat to the joint and measures to deal with the source of infection Complete immobilization of the joint is neither necessary nor wise. After a few days rest the patient should be encouraged to begin active joint movements. Heat can be applied in the form of Antiphlogistine poultices, infra red irradiation, diathermy or short wave diathermy Counter irritation by Scott s dressing or Iodex ointment and an elastic *crêpe* bandage can also be used

General treatment will include a course of a sulphonamide, preferably combined with T.A.B fever therapy followed by a course of injections of polyvalent gonococcus vaccine. The source of infection will be dealt with on routine lines After the acute stage has passed and swelling has subsided usually in from one to three weeks a course of massage and remedial exercises can begin The joint must be kept mobile throughout This does not delay resolution and avoids the possibility of adhesions

Tenosynovitis and myositis alone, or in association with a joint affection are treated on the same general lines. Tenosynovitis is characterized by pain on movement and redness over the affected tendons. The ankle and wrist regions are common sites Fascial inflammation occurs particularly about the feet, causing painful heels and soles and sometimes a dropped arch It is liable to be more resistant to treatment than almost any other form of rheumatism

Acute General Affection When a number of joints, tendon sheaths and fasciae are affected the condition of the patient is often serious. There is an associated toxaemia with swinging temperature prostration general wasting and anaemia Iritis quite frequently occurs at the same time and keratoderma blennorrhagica is found oftenest in this type of case. The complement fixation test is sometimes negative possibly because there is a lack of antibody response to the infection.

The patient s general condition should be improved before any drastic means of treatment are tried but a course of a sulphonamide and gonococcal vaccine can be begun at once

Large doses of iron are given for the anaemia, and heat and general massage with movements are used for the joints. Fever therapy should be withheld until the general condition has improved but gives very good results The focus of infection in the genito-urinary system must be sought out and treated The joints must be kept moving by both active and passive means, for adhesions form easily in such cases and the patients are apt to degenerate into a condition of chronic invalidism. The various physio-therapeutic methods of treatment are used in the convalescent stage.

Tests for cure must be long and searching for relapse is common if the genito-urinary infection is not eradicated A subsequent gonorrhoea is almost certain to provoke another attack of polyarthritis which may be even worse than the first. Even if the greatest care is taken, adhesions may occur in or about the joints and will require treatment by an orthopaedic surgeon.

Chronic Arthritis Chronic joint affections may follow an acute attack of monarticular or polyarticular rheumatism, but the condition may be chronic from the start. Transient subacute arthritis of a joint or joints is not uncommon with a latent gonococcal infection and a persistent polyarthritis of the rheumatoid type may be due to this cause. Iritis sometimes coincides or alternates with exacerbations of rheumatism. Chronic tenosynovitis, fascitis and myositis are less common Chronic rheumatic conditions, particularly when they have not been preceded by an acute attack, coming long after a gonorrhoea, offer great difficulty in diagnosis and sometimes, in spite of a most careful search, the only evidence pointing towards gonorrhoea is a positive complement fixation test

Treatment consists of vaccine and fever therapy with eradication of the source of infection if it can be discovered Sulphonamides should be tried, but the results are not likely to be as good as in acute cases Massage, movements and the application of heat by various physio-therapeutic means are used locally Hyperthermy sometimes gives good results

Chapter VI

VULVOVAGINITIS IN CHILDREN

The vulva and vagina are much more liable to infection before puberty when their columnar epithelium changes to the more resistant squamous type. After puberty too there is further local protection against infection in the more acid reaction of the vagina and the presence of Döderlein's bacilli in the vaginal flora The gonococcus is an important though not the commonest cause of vulvovaginitis. Infection may occur at any time from birth to puberty but is commonest in the *middle years of childhood* The incubation period is about *four or five days*

GONOCOCCAL VULVOVAGINITIS

Infection is generally accidental through contact with towels and sponges, bed linen or lavatory seats contaminated with infectious material An infected adult can usually be found in the house and parental infection is often to blame Investigation of a case should always include examination of male and female contacts in the child's home In institutions epidemics can occur being spread by the articles named above and by bed pans, nurses aprons thermometers etc Assault is rarely responsible for infection in Great Britain In this connexion some assaults are provoked by a quite commonly credited belief that gonorrhoea in the male can be cured by intercourse with a healthy young female.

Diagnosis

The child may be brought for examination because of complaints of burning or irritation or because discharge has been seen on her clothing The vulva is red and irritated and pus is seen to ooze from the urethral and vaginal orifices The rectum may be affected and then there is redness of the anal orifice and a mucoid or purulent discharge Both smear and culture tests of material from the urethra vagina and rectum should be used to confirm the diagnosis It is im

portant to have an accurate pathological diagnosis, particularly in cases of assault

Complications

These are fortunately rare, but the child is liable to much the same complications as the adult. They include proctitis, cervicitis, endometritis and salpingitis, peritonitis, conjunctivitis, rheumatism, iritis and septicaemia.

Treatment

Cases of vulvovaginitis should always be treated in institutions catering especially for the work and employing specially trained personnel The nursing is most important and the following are salient points in general conduct. They are taken from the rules of the London County Council special hospitals.

1 Nurses must wash the hands carefully after treating each case.
2 Aprons or overalls can spread infection, so each patient must have a separate piece of mackintosh which can cover the nurse's lap when she attends to the child. Individual towels are essential
3 A separate thermometer should be provided for each patient and temperature only taken in the axilla or mouth.
4. Baths with running water are least liable to spread infection
5. Separate bed pans and chamber-pots must be provided for each case
6 Children are not allowed on another patient's bed

(1) *The Sulphonamides* The results with sulphonamide treatment are very good and have reduced the time under treatment enormously Dosage is regulated according to age. Infants under one year can be given a quarter tablet (⅛ gm.) four times daily for from five to seven days. Children from one to five years will tolerate half-tablet (¼ gm) doses in the same period and over fives will take one-tablet (½ gm) doses Sulphapyridine is effective but sulphathiazole or sulphadiazine are much better supported.

(2) *Local Treatment* The child should be confined to bed and isolated for the first two or three weeks With sulphonamide treatment local hygiene is often all that is necessary The child is kept clean by frequent baths and the vulva is

swabbed with a mild antiseptic lotion such as 1 1000 solution of Acriflavine in glycerine followed by an application of dusting powder Discharge dries up very quickly

If clinical or pathological relapses occur the focus of infection must be sought and treated and a further course of a sulphonamide may be necessary Douching is rarely needed, but where it is necessary ½ per cent solution of Protargol can be used Resistant cases may sometimes need vaginal swabbing and 5 per cent mercurochrome in glycerine is commonly used It is applied on a dressed probe and a urethroscope cannula can be used if necessary as a speculum Polyvalent vaccines are used in complicated cases with good results

Oestrin has given satisfactory results in some cases particularly in pre-sulphonamide days Its effect is to cause a change in the epithelium to the adult type. Oestrin can be given by injection by mouth and by vaginal suppository Oral administration is the best as it causes least upset to the child The daily dose is from 3000 to 6000 units

Follow up must last for six months and include smear and culture tests from urethra vagina and rectum weekly at first but with longer intervals later The complement fixation test should be done at the start and must be negative at final test

NON-GONOCOCCAL VULVOVAGINITIS

This is commoner than the gonococcal type, and usually occurs between the ages of two and ten years It may coincide with acute specific infections such as the infectious fevers, *pneumonia and influenza with general debilitating diseases* and with acute throat infections due to streptococci diphtheria or Vincent s organisms

Local causes are foreign bodies irritation by clothing or by masturbation and direct infection by dirt or fomites Threadworms, chronic constipation appendicitis and renal affections may also cause an associated vulvovaginitis

These cases are best treated in hospital and gonorrhoea must be excluded by careful investigation The majority will clear up after removal of the cause, with local hygiene by bathing and local applications as described under gonorrhoea Sulphonamides may be necessary in resistant cases

CHAPTER VII

URETHRAL STRICTURE

NARROWING of the lumen of the male urethra due to fibrosis in the wall may follow a variety of causes including gonorrhoea internal trauma from stones or foreign bodies in the urethra or external trauma Congenital stricture is also known In gonorrhoea stricture may be due to infiltration and subsequent organization of the sub-mucous tissues or may follow a para urethral abscess. Post-gonorrhoeal stricture is commonest in the bulbous part of the urethra, but may occur anywhere from the fossa navicularis to the membranous urethra Stricture in a well-handled case of gonorrhoea is almost unknown, but in the past many strictures were caused by the injudicious use of instruments in the treatment of acute gonorrhoea

The early diagnosis of stricture or potential stricture will be made during the follow-up and tests for cure for gonorrhoea. The use of a sound or urethroscope in the test of cure will reveal by touch or to the eye, any narrowing in the passage Loss of elasticity or inflatability during urethroscopy is suspicious Any case of gonorrhoea which was complicated by a para urethral abscess is instrumented during follow up tests and final discharge as cured is delayed for six to twelve months to ensure that subsequent narrowing has not occurred

Diagnosis

Stricture may come to notice by an attack of acute retention of urine or because of increasing difficulty in urination with small stream, dribbling and forcing at the start. Acute retention may be precipitated by congestion due to an acute gonorrhoea on top of a stricture, or to exposure to cold or a bout of alcohol. This must be distinguished from congestion due to para-urethral abscess, prostatic or vesicular abscess or to enlargement of the prostate gland The symptoms of established stricture have also to be distinguished from those due to prostatic enlargement urethral calculus and nervous diseases such as tabes dorsalis which affect bladder function.

Treatment

(1) *Stricture with Acute Retention.* The effect of heat is first tried by putting the patient in a hot bath and having him try to urinate while immersed The patient may be given ¼ grain of morphia by injection before the bath If no result is forthcoming after a few hours and the bladder is becoming distended, the urethra is irrigated with a 1 10 000 solution of mercury oxycyanide and an attempt is made to pass a rubber catheter starting with a medium size and working down This is effective in most cases, but a few will have to be tried with gum elastic catheters

Catheters are well lubricated along the whole length with a sterile lubricant such as liquid paraffin If catheterization is impossible a filiform bougie can sometimes be passed and the patient may be able to pass water around it Special filiform instruments to which a catheter can be attached are also obtainable If the filiform bougie is passable it acts as a guide to direct the attached catheter through the stricture and curls up inside the bladder when the catheter is passed

If relief cannot be obtained by instruments, the patient should be admitted to hospital for a suprapubic cystostomy but if this is impossible, in an emergency the bladder can be *punctured suprapubically with a trocar and cannula and the* urine drawn off slowly A prepared cystostomy is best in the first instance if at all possible The operation is followed by instrumental dilatation of the urethra before the patient leaves hospital and treatment is continued as an out patient

(2) *Established Stricture* Often the face of a stricture can be seen with the urethroscope and this is a great help for by defining the position of the orifice subsequent instrumentation is facilitated The Campbell urethroscope has a side passage by means of which a filiform bougie can be passed under direct vision The extent of a stricture varies from a short local narrowing to quite a considerable length of fibrosis. More than one stricture may exist in different levels of the urethra. The best method of treatment is by a gradual dilatation at frequent intervals until a medium-size bougie can be passed easily when the frequency of treatment can be reduced according to the rate at which the stricture contracts down again.

Patients must be warned to keep constantly under observation until it is definitely established that the stricture is completely quiescent and fully dilated

At the first treatment it is well to begin operations with a moderate-sized instrument such as a 12–14 gum elastic bougie and work downwards if unsuccessful. Force must never be used or trauma and false passages are a result. Steel sounds are best left to experts in the first instance, as trauma is likelier than with gum elastic instruments If the ordinary gum elastic bougies cannot be passed, it may be possible to find the orifice by putting down half a dozen filiform bougies, when one may strike the orifice. In such a case the filiform is left *in situ* for twenty-four hours. The patient naturally is in bed. He can pass water past the bougie and has little discomfort. Afterwards it is possible to use larger instruments. Filiform bougies to which a larger bougie can be attached are very useful in such cases.

At first one session a week is necessary but as the passage gets larger the interval is extended gradually to two weeks, four weeks eight weeks, and twelve weeks between treatments. It is best to irrigate the urethra with 1 10 000 solution of mercury oxycyanide both before and after instrumentation. In most cases there should be little or no bleeding once the operator has learnt the idiosyncrasies of a particular urethra. It is best for one person always to handle a stricture, for he will get to know its contours. Once the stricture is well dilated, steel sounds such as Lister's or Clutton's can be used. Lister's are better for tortuous strictures

Passing a Metal Sound. The operator stands at the right side of the patient and, holding the sound horizontally and with the point downwards introduces it from the side and downwards until the point is nearly at the bulb. The handle is then brought up vertically and turned so that the curve of the instrument corresponds with the line of the urethra. Gentle pressure backwards and downwards, pressing the handle between the patient's legs will cause the point of the instrument to pass into the bladder The handle should go right up to the meatus. A finger in the perineum assists and guides the operator in some cases The point of the instrument is kept to the roof of the urethra as it passes.

In all cases where instrumentation is difficult, the practi-

tioner will be well advised to have the assistance and advice of a venereologist or genito-urinary surgeon in the first instance.

Operative Treatment. A passable stricture which is fairly small in extent can be treated by incision with the internal urethrotome followed by instrumental dilatation. Complete excision of a stricture is possible in certain cases The selection of cases suitable for operation must be left to a genito-urinary surgeon

Complications of Stricture Abscess formation fistula and extravasation of urine behind a stricture are possible complications which will require surgical intervention Such cases are not suitable for treatment in general practice and a specialist s opinion should be sought at once

Meatotomy may be necessary if a small meatus makes passage of instruments difficult This is easily done under local anaesthesia. The meatus is slit anteroposteriorly with a sharp narrow scalpel or meatotomy knife. Subsequent contraction is avoided by dilatation of the orifice with sounds

GENERAL INSTRUCTIONS FOR INSTRUMENTATION

Irrigate the urethra first with 1 10 000 solution of oxycyanide of mercury and cleanse the end of the penis with methylated spirit before instrumentation

Use soft instruments, rubber or gum elastic catheters first in cases of retention of urine in order to avoid trauma.

No force must be used in urethral instrumentation

Sterilize rubber and steel instruments by boiling gum elastic by formalin vapour

Wash instruments after use

Lubricate with a sterile lubricant all along the instrument to make for least pain to the patient and greatest ease in introduction

CHAPTER VIII

THE SULPHONAMIDES

HISTORY

SULPHANILAMIDE was first synthesized by Gelmo in Vienna in 1908, but no clinical trials were then made. Clinical reports on the sulphonamides first appeared in Germany in 1933 and 1934, but not until Domagk's work with Prontosil in streptococcal infections was published in 1935 was the importance of this group manifest.

In 1936 *p*-benzyl-aminobenzenesulphonamide (Proseptasine, May and Baker) appeared. This was active against haemolytic streptococcal infections and less toxic than sulphanilamide. Sulphapyridine (May and Baker 693) was first reported in 1938 and sulphathiazole (May and Baker 760) dates from about *the same time, although its general use was not* possible until much later.

Sulphaguanidine, used for bacillary dysentery and other intestinal infections, appeared in 1940, as did sulphadiazine. Sulphamethazine *was made available in 1941*.

These are the landmarks in the development of the sulphonamides, but very many other derivatives have been prepared and tested during this time. Many have given therapeutic results of a varying degree of success. The drugs mentioned are among the most prominent in a long series of investigations.

MODE OF ACTION

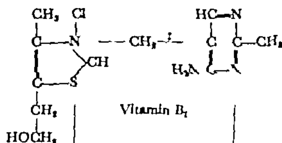
The sulphonamides appear to exercise their effects in infections not by any direct action on micro-organisms or by increasing tissue resistance but by interfering with the internal metabolic processes of bacteria. The sulphonamides are similar in structure to para-aminobenzoic acid and it is probable that, when the concentration in the tissues is sufficient, a sulphonamide can pre-occupy some cellular enzyme which normally functions in metabolism by an action on para-aminobenzoic acid.

Sulphonamide resistance, or fastness, can be produced by

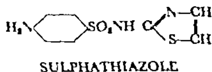
THE SULPHONAMIDES

SULPHANILAMIDE

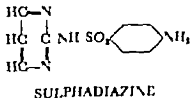




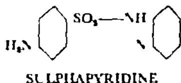
Vitamin B_1



SULPHATHIAZOLE



SULPHADIAZINE



SULPHAPYRIDINE

low dosage which gives a tissue concentration of the drug insufficient to kill all the bacteria Resistant strains of gonococci have been isolated, but it has not been conclusively proved that resistance is maintained on transmission to another host. In the production of drug resistance it is probable that a number of factors in the host, bacteria and drug are concerned other wise all cases should be cured by adequate dosage A strain of gonococci resistant to one sulphonamide is theoretically resistant to all, but in practice the resistance is seldom complete and a change of drug is often effective, particularly when the action is enhanced by an induced fever

The action of penicillin is not affected by a previous sulphonamide resistance.

GENERAL DESCRIPTION

In the text, standard lines of treatment with the common available sulphonamides have been laid down. The methods chosen are ones which have been used in large numbers of cases with good results and which can be taken as the best for the average case. Very many different schemes of treatment have been tried varying the dosage and the times over which, and at which the drug is administered Some of these different methods which have proved successful will be outlined under the different drug headings, for they may be applicable in special instances. Toxic effects of the sulphonamides and their treatment will also be described.

With most sulphonamides the best results are obtained by heavy dosage in the first forty-eight hours, when the main action seems to take place. Prolongation of therapy over seven days in one course is usually a waste of time and drug In hospital practice it appears that four hourly administration throughout the twenty-four hours gives the best results but this is impractical in out patients, and little is lost by omitting the night dose and spreading it over the day It is widely agreed that the combination of a sulphonamide with local treatment will give results superior to either method alone. Throughout the sulphonamide series a high fluid intake is absolutely essential if toxic effects are to be avoided

Low initial dosage leads sometimes to a condition of drug fastness in which the gonococcus becomes very resistant to

chemotherapy In such cases it is useless to try the original drug again, but another sulphonamide alone or with fever and vaccine therapy may be successful. Treatment with penicillin is rapidly effective in almost all cases of uncomplicated sulphonamide resistance. Should penicillin fail, hyperthermy alone or combined with sulphonamide or penicillin therapy is the last resort

SULPHAPYRIDINE (M & B 693)

As already described under the treatment of acute gonorrhoea the average dose is about 25 gm spread over 5–7 days. Other schemes which have been used are—

(1) 6 gm. daily for 4 days given in 1 gm. doses every 4 hours.
(2) 5 gm. daily for 5 days
(3) 10 gm in a single massive dose.

All three schemes give best results on bed patients. The results in the first two instances are comparable with those obtained on the schemes already described in the text, about 90 per cent of uncomplicated acute cases reacting without further chemotherapy The results with massive dosage of sulphapyridine are less satisfactory for although a high percentage of acute cases reacts well those which fail are far more difficult to cure than failures treated by more prolonged courses. Vomiting is commoner too with massive dosage, and this, of course necessitates a return to a scheme of spread dosage.

Drug rash is very rare and renal toxicity does not occur with massive dosage Chronic gonorrhoea is quite unaffected by massive doses of sulphapyridine or indeed of any sulphonamide

With scheme (1) above renal complications are apt to arise if the very closest attention is not paid to the fluid intake or if complete immobility is not ensured

Sulphapyridine has also been used by intramuscular injection The results obtained were not encouraging and the injection is often extremely painful even if a local anaesthetic is used first The dosage by this method is 1 gm. of a sterile suspension of sulphapyridine in distilled water daily for four days. Soluble sulphapyridine diluted with twice the quantity of sterile normal saline solution can also be given in 1 gm doses

intravenously Both these injection methods are available for trial when persistent vomiting interferes with oral administration, but the results are not spectacular and in such cases it is best when possible to change to sulphathiazole or sulphadiazine.

Toxicity

Minor toxic effects of dizziness, headache, general depression and nausea are very common with sulphapyridine particularly in heavy dosage and at the start. These symptoms may pass off while the drug is continued and are not to be interpreted that dosage should be reduced or stopped. Vomiting is not uncommon particularly with out-patients, and can sometimes be avoided by taking the crushed tablets in milk, in an emulsion or by giving sodium bicarbonate at the same time. The best plan, however is to change to sulphathiazole or sulphadiazine at once, if one or the other is available. Drug fever is not very common and should be diagnosed only in the absence of complications of gonorrhoea. It occurs generally from the fourth to the seventh day but may be earlier Oedema of the face or even general oedema may coincide, and this is one of the reasons for an immediate cessation of treatment.

Rashes, scarlatiniform or morbilliform in character occur on or about the eighth day after the start of treatment and are commonest when long courses are used A rash alone does not mean that treatment must cease, and signs usually disappear spontaneously in forty-eight hours or so Agranulocytosis occurs in some instances and is likeliest if prolonged courses are given. Haematuria and anuria can occur in even the best watched cases, but with prompt treatment fatalities are now fortunately rare.

SULPHATHIAZOLE (M & B 760, CIBAZOL)

This, or sulphadiazine, will be the drug of choice if available. It is well tolerated in any dosage by bed- or out patients and minor toxic effects are very rare The major toxic effects are the same as those encountered with sulphapyridine and occur in about the same proportion of cases. A high fluid intake is essential when sulphathiazole is used

Apart from the suggested routine of 6 gm daily for four

TOXIC EFFECTS OF THE SULPHONAMIDES IN COMMON USE

Phenomena	Sulphanilamide	Sulphapyridine	Sulphathiazole	Sulphadiazine
1 Cyanosis	Very common. Often with no other symptoms. Continue treatment	Fairly common, but never marked. Continue treatment	Rare	Rare
2 Dizziness	Common. Continue treatment	Common. Continue treatment	Rare	Rare
3. Nausea and vomiting	Common in out-patients. Change drug	Common in out-patients. Change drug	Rare	Rare
4. Fever	Not very common. Stop drug if persistent	Not very common. Stop drug if persistent	Not very common. Stop drug if persistent	Rare
5. Rash	Fairly common with 7-day or longer courses. Occurs about 8th day—scarlatiniform or morbilliform	As with sulphanilamide	Uncommon	Rare
6. Leucopenia	Not uncommon if looked for. Do blood count always before 3rd course of any drug	Not uncommon	Not uncommon	Rare
7 Agranulocytosis	Uncommon. Occurs 7th–25th day	Uncommon. Occurs 17th–25th day	Rare	Rare
8. Haemolytic anaemia	Uncommon. Severe type occurs about 5th day with pallor and jaundice	Uncommon	Rare	Rare
9. Haematuria	Does not occur	Clinical haematuria uncommon. Pathological haematuria fairly common	Uncommon	Rare
10. Anuria	Does not occur	Uncommon. Usually with heavy doses and insufficient fluid	Uncommon. With heavy doses and insufficient fluids	Rare

If diagnosed, stop drug at once and force fluids.

ULERON

This drug is mentioned because it has been used to a large extent on the Continent, particularly in Germany The recommended dosage was two or three courses of 3 gm daily for four days, with a week between courses. The results were not comparable with those now obtained with sulphapyridine and the later sulphonamides The usual toxic effects were noted but the most important was peripheral neuritis. This followed over-dosage, in quantity or in time, was sometimes very severe, and resulted in paresis or paralysis of the lower extremities.

TOXIC EFFECTS OF THE SULPHONAMIDES

A very large number of toxic phenomena has been reported as occurring during sulphonamide treatment Some are common to all the sulphonamides others are particular to one or two The common and important toxic manifestations are tabulated on page 98

Apart from those shown in the table, the following are effects which have been noted, but more rarely with one or all of the sulphonamides

Albuminuria	Psychosis
Neuritis	Acidosis
Hepatitis	Injection of the sclerae and conjunctivae
Purpura	
Ocular and auditory disturbances	Peripheral vascular failure
Stomatitis	Diarrhoea or intestinal haemorrhage
Painful joints	

All these are indications for the cessation of treatment and the forcing of fluids. It was also suggested at one time that the sulphonamides had an injurious effect upon the production of spermatozoa, with consequent sterility This has been disproved. Sulphadiazine is rarely incriminated as a cause of the above or of any toxic effects By ensuring a very high fluid intake during chemotherapy the possibility of toxic effects is very markedly reduced

MINOR TOXIC EFFECTS

These are best avoided by using sulphathiazole or sulpha diazine, but if for any reason sulphapyridine or sulphanilamide are being used, they can be minimized by keeping the patient in bed Nausea and vomiting can be reduced by keeping the patient unaware of the possibility and by giving the tablets crushed in milk or as an emulsion

Rashes usually occur about the eighth day when treatment will generally have ceased They are not common on the short courses recommended in the chapters on treatment. The character of the rash is commonly scarlatiniform or morbilli form and may be localized on the limbs or face but is usually widespread A low fever often accompanies a rash Many a patient is admitted to a fever hospital with a mis-diagnosed sulphonamide rash The opposite too happens when a secondary syphilide in a patient taking a sulphonamide is diagnosed as a drug rash. Sun bathing must be prohibited in patients on sulphonamide treatment as rashes are often thereby precipitated If itching is troublesome calamine lotion with 2 per cent phenol can be used but generally nothing is needed and the rash fades in 24–48 hours Treat ment need not cease if a rash appears near the end of a course, but if fever is also present fluids should be forced and the drug suspended

A slight transient fever need cause no alarm if fluids are kept up and if there are no other toxic manifestations.

MAJOR TOXIC EFFECTS

(1) *Leucopenia.* Leucopenia with granulocytopenia may be discovered by routine blood counts before further medication in certain cases of sulphonamide-resistant gonorrhoea. If the total white-cell count falls below 4000 or the granulocytes are under 50 per cent further sulphonamides are absolutely contra indicated and the case must be carefully watched As a precaution injections of liver and Pentnucleotide may have to be given.

(2) *Agranulocytosis* —This condition is characterized by marked granulocytopenia with faucial ulceration. Sulphon amides must stop at once if this condition is suspected Specific

treatment consists of injections of 0 7 gm Pentnucleotide twice daily and of 2 c.c. of a parenteral liver preparation every other day continued until the granulocyte count begins to rise. The Pentnucleotide injections are then reduced to one daily until the granulocyte count is normal

(5) *Haemolytic Anaemia* A slight degree of anaemia some times follows sulphonamide therapy and is easily controlled with iron. An acute anaemia of sudden onset early in treat ment, with pallor and jaundice, is less commonly seen. Blood transfusion may be necessary Good results are reported with parenteral liver therapy and iron in the less severe cases

RENAL COMPLICATIONS

Haematuria is a fairly common and very important complication of treatment with sulphapyridine and sulphathiazole. It is rather less common with sulphadiazine and it does not occur with sulphanilamide. The description which follows covers all three drugs.

Dr S M Laird (*Lancet*, Sept. 1941 p 272) has made a good summary of the three common clinical types of cases encountered

(1) Haematuria. This is only detected by microscopical examination of the urine It is sometimes accompanied by back or abdominal pain.

(2) Gross haematuria with back or abdominal pain relieved by withdrawal of drug and forced fluids.

(3) As in type (2) but not yielding to conservative treat ment and going on to anuria and nitrogen retention. Such cases if untreated, have a fatal outcome

Haematuria is produced by the irritative action of crystals of acetyl sulphapyridine in the renal tubules, pelvis and ureter Sulphapyridine is excreted in the urine, partly unchanged and partly as the acetyl derivative, and precipitation of the sharp crystals of acetyl sulphapyridine is favoured by a high dosage, inadequate fluid intake and by an unassessable metabolic factor in each patient which governs the amount of drug ex creted as the acetyl derivative The crystals produce mechani cal trauma of the tubules, pelvis and ureter with oedema and, possibly ureteric spasm In cases of type (3) the combination of spasm and mechanical obstruction of the ureters by blood

clot and crystals results in hydronephrosis anuria and nitrogen retention.

The case with gross haematuria may not at first seem very ill but there is commonly a complaint of pain in the loins, flanks or over the bladder There may be vomiting both before and with the haematuria, and this may in fact be a cause of lowered fluid intake The urine contains blood and crystals of acetyl sulphapyridine. If there is no response to treatment the general condition becomes very bad Nitrogen retention becomes clinically evident and the patient may be comatose Pain persists and there is often fever

Treatment

Prophylactic treatment will prevent the majority of cases The fluid intake must be maintained at more than six pints a day and a careful watch kept on the urine At the first sign of haematuria the drug must be stopped at once and fluids forced Hot poultices should be applied to the loins and morphia may be necessary if pain is severe. If the patient is unco-operative or if there is much vomiting and output of urine is low intravenous 5 per cent glucose and saline must be given In the majority of cases, if taken early these measures will soon restore the urinary output to normal and the haematuria will disappear If however there is evidence of nitrogen retention and anuria or gross diminution in urinary output, the patient should be admitted to hospital for cystoscopy and ureteric catheterization There is no reason to delay this simple measure and it should definitely be done within twelve hours of the establishment of anuria The actual passage of the ureteric catheters is sometimes difficult as the ureteric orifices may be oedematous Passage of the ureteric catheter may dislodge some clot from the orifices and pain is sometimes relieved at once

The catheters should be left *in situ* for 12 to 24 hours Once they are inserted the renal pelves can be washed out with a few c cs of normal saline and flow usually starts at once Fluids are given by mouth and by intravenous drip if necessary but once complete anuria is established it will be wise to curtail fluids until catheterization has been done or more kidney damage may be produced In the very rare cases where ureteric catheterization is impossible recovery

has been noted after unilateral nephrostomy and drainage.

Dr W A. Flynn has described a method of treatment of cases of haematuria where the onset of anuria is feared. In conjunction with the administration of fluids, massage of the abdomen over the kidneys and ureters is performed for two to three minutes on each side and the lower ends of the ureters are agitated by massage per rectum The result may be that the combination of fluid pressure and agitation of the ureters may dislodge crystals and clot and free the passage.

The rationale of this treatment is confirmed by observations that patients with sulphonamide anuria conveyed by bumpy ambulance from one hospital to another for surgical intervention recovered in transit.

It is generally unwise to resume sulphonamide treatment in cases which have had haematuria unless there is an urgent reason for it. In such cases a different sulphonamide should be used the initial dosage should be very small and the case should be carefully watched so that treatment may cease at once if there is a recurrence of symptoms of renal intolerance.

SULPHONAMIDES AND PENICILLIN

It was early suggested that concurrent exhibition of penicillin and a sulphonamide resulted in a synergistic action against the gonococcus My own investigations on considerable numbers of cases do not support this suggestion. When adequate dosage of penicillin is employed the concurrent use of sulphonamide therapy in uncomplicated gonorrhoea is unnecessary

The sulphonamides are useful and often effective in cases of gonorrhoea where a residual discharge (containing no gonococci and presumably due to secondary infection) persists after penicillin treatment.

Chapter IX

PENICILLIN TREATMENT OF GONORRHOEA

Penicillin is the most rapid and effective remedy yet discovered for the treatment of gonorrhoea. Its efficacy is little affected by the duration of the disease, provided there are no complications, or by previous medication with other remedies.

The use of penicillin in gonorrhoea is contra indicated only if a patient should also be suffering from an undiagnosed ulceration of the penis. In such cases it is wiser to use a sulphonamide until the diagnosis has been established

Toxic effects are rare but transitory erythematous or urticarial eruptions sometimes occur usually in patients who have been sensitized by previous medication with penicillin. Patients sometimes complain of local pain from injections of certain batches of penicillin in aqueous solution and oil wax suspensions frequently give trouble in this way

Cases in which penicillin fails entirely to cure uncomplicated gonorrhoea are rare but I have had one case (and others have been reported) in which gonorrhoea still persisted at the end of treatment with 2,400 000 units for coincidental syphilis.

ACUTE GONORRHOEA

The usual sequence of events in cases of acute gonorrhoea adequately treated with penicillin is as follows gonococci begin rapidly to degenerate and disappear from secretions in from 8 to 24 hours urethral discharge in men disappears in from 2 to days and is often enormously reduced within a day the urine lears in 2 to 7 days although a few threads or flakes may persist for some weeks.

Relapse may show itself in several ways discharge may diminish for a day or two and then increase with a reappearance of gonococci discharge may cease completely and then recur after a lapse of from a few day to a month (reinfection is more likely after this time epididymitis or some other complication may appear usually after a lapse of some weeks, but sometimes within a fortnight

Acute gonorrhoea in women usually reacts to treatment with the same dosage as suggested for men.

Treatment

Penicillin alone will cure more than 80 per cent of cases of acute or sulphonamide-resistant uncomplicated gonorrhoea without any adjuvant treatment. The dosage required is at least 100,000 units in aqueous solution in divided doses or at least 200,000 units in oil-wax suspension in a single injection. Single injections of large doses in an aqueous solution are not trust worthy and oral administration is inefficient and wasteful of penicillin.

The most reliable method of administration is by divided doses in aqueous solution given every two or three hours for four or five doses. The total dosage should be 200,000 units given as four injections of 50 000 units at intervals of three hours, or as five injections of 40,000 units every two hours. An alternative method almost as good, is to give one injection of 100 000 units followed by two of 50 000 units at intervals of four hours. The method chosen will depend on the availability of the patient.

When the patient cannot attend frequently for injections, a single injection of 300 000 units penicillin in oil-wax suspension can be given.

Patients should be examined the day after treatment and then every other day until all discharge has ceased and the urine is clear — usually about one week in successful cases. They should then follow the routine shown for follow-up of acute gonorrhoea. A final blood test is done six months after treatment to exclude any possibility of missing a case where syphilis may have been suppressed by penicillin and not recognized at the test done three months after treatment.

Adjuvant Treatment

When the physician has facilities for irrigation the disappearance of signs and symptoms may be hastened by daily anterior lavage with 1 10,000 potassium permanganate solution for the first few days.

Irrigation is also useful for those cases in which a slight mucoid discharge persists at the end of a week after treatment.

When a profuse discharge, containing no gonococci, persists

after treatment a course of a sulphonamide and irrigations should be used, and the case handled on the lines suggested for non-gonococcal urethritis. Failure to respond to this treatment is an indication to try penicillin again

In women, if discharge is profuse sodium bicarbonate douches can be used for a few days. If a *Trichomonas vaginalis* infestation coexists, it must be treated in the usual way as penicillin has no effect on this organism

Relapse In any case where relapse (with reappearance of gonococci) occurs whether this be soon or late after treatment, a careful search should be made for any focus of infection for example, in para urethral ducts, prostate gland, etc. If no such focus is discovered the case should be treated again with penicillin, the total dose being raised by 50 per cent and divided into at least four injections at 2 or 3 hourly intervals. (Penicillin in oil wax suspension is not recommended for treating relapsed cases.) The majority of relapses will react to this treatment.

In very few instances is there a subsequent relapse, and then, in the absence of any complication, the following procedure is indicated 200 000 units penicillin are given by four or five divided doses on each of two successive days. If even this is ineffective, a course of twenty injections, each of 50 000 units, every three hours, can be tried

For the extremely rare case which does not yield to penicillin in any dosage, sulphonamides (with fever therapy) or as a last resort hyperthermy can be used

COMPLICATIONS OF GONORRHOEA

The duration of infection in gonorrhoea provided there are no complications has no bearing upon the efficacy of penicillin

In the presence of complications penicillin is not always so spectacular in its effects as it can be in acute gonorrhoea With closed foci of infection penicillin often fails sometimes because of inadequate dosage In cases of frank abscess formation for example, para urethral or Bartholin's gland abscess, penicillin given before the abscess has been drained is usually wasted. Surgical treatment should then precede penicillin treatment, and good results can be expected Local treatment for complications is given in the usual way as well as penicillin

As a general principle, it is wise to give larger doses of penicillin in complicated than in uncomplicated gonorrhoea. Penicillin treatment does not mean that follow-up tests can be any less rigorous than was usual in the past for complicated gonorrhoea.

Prostatitis

Penicillin should be given at once in cases of acute prostatitis, in total dosage of 900 000 units in five 3 hourly injections. Even so, abscess formation may occur and treatment has to be repeated when drainage has been established surgically or otherwise. Prostatic massage is usually necessary in after treatment, as already described.

Epididymitis

The course of this complication (so far as local pain, etc. is concerned) is unaffected by penicillin treatment. Penicillin should be given at once, as in prostatitis, and repeated if there should be any local relapse or reappearance of gonococci in urethral secretions.

Rheumatism

Gonorrhoeal arthritis and rheumatism seldom react any better to penicillin than to other remedies used in the past. Local foci of infection must be carefully sought out and given appropriate treatment. Penicillin should be used in large doses if it is to be useful for example, sixty injections, each of 50,000 units, 3 hourly for 7½ days.

If a case of arthritis proves resistant to penicillin and the simpler remedies, there should be no delay in using hypertherm treatment if this can be arranged.

Gonococcal Abscesses

If a patient, male or female, presents with a superficial abscess (peri- or para-urethral, of Cowper's or Bartholin's gland) it is best to produce drainage before penicillin is given. The dosage used can then be as for prostatitis. When such a case is seen, in which it is doubtful whether pus has formed, it may sometimes be possible to abort the condition by the use of penicillin in large doses continued over several days. It is my opinion that, even there, it is best to apply local heat until the abscess is ripe, incise, and then use penicillin.

Salpingitis

Good results are reported from the treatment of acute salpingitis with penicillin in large doses, for example, 50,000 units, 3 hourly over 3–7 days. In chronic cases penicillin should be tried, but the percentage of successes is not so high. Careful follow up is important, and local treatment must not be neglected. Surgical treatment is still sometimes necessary.

Septicaemia and Endocarditis

The treatment advised for bacterial endocarditis caused by penicillin-sensitive organisms is with large doses, 50 000 units and more, 3 hourly over 21–28 days.

Conjunctivitis

Sorsby reports excellent results in ophthalmia neonatorum (gonococcal or otherwise) with local instillation of penicillin solution. He recommends washing the eye clean with half strength saline and then instilling two drops of a solution of penicillin (2500 units per c c) every minute for 20–30 minutes, when all tendency to pus formation is suppressed. Instillation is then continued every five minutes for half an hour, half hourly for three hours, hourly for six hours, and then two-hourly for a further twelve hours. In my opinion this treatment should be reinforced by parenteral penicillin in the dosage used for acute gonorrhoea in the adult.

Gonorrhoeal (and meningococcal) conjunctivitis in the adult should be treated on similar lines with local and parenteral penicillin. Two adults treated personally with parenteral penicillin and only saline irrigations locally cleared up with astonishing rapidity.

Any case with ocular complications should be treated in hospital from the start.

Vulvo-vaginitis in Children

This condition is reported to react in the majority of cases to penicillin in the dosage used for adults. Children should still be hospitalized for treatment.

Masking of Syphilis

Penicillin is the first remedy which has been found effective against both the gonococcus and *S pallida*. There is therefore

a theoretical possibility that its use in gonorrhoea in cases in which a syphilitic infection has been coincidentally acquired may delay the appearance of signs or even suppress the early lesions of syphilis entirely. The incubation period of syphilis is indeed lengthened in such cases but there is no evidence, so far that a state of latency in syphilis can be produced by the doses normally used in uncomplicated gonorrhoea.

In no case that I have seen personally has the appearance of surface lesions of syphilis been delayed by penicillin treatment of gonorrhoea beyond three months—the usual follow-up period in the past. The incubation period is sometimes unaffected but in my experience it has usually been lengthened, the average being to about fifty days. The practice, now nearly universal, of having patients attend for blood tests for syphilis at six months after treatment, as well as at three months, should ensure that no double infections are missed.

The problem is much more important in gonorrhoea where relapse or complications make necessary the use of larger doses of penicillin given over longer periods. In such circumstances, where doses of 1,000,000 units or more may have to be given, there is a case for giving enough penicillin to be effective in any syphilitic infection which may coincide, that is, 3,000,000 units or more.

PART II

SYPHILIS

CHAPTER X

INTRODUCTION

SYPHILIS is a specific infectious disease caused by *Spirochaeta pallida* and confined to the human race. Infection can occur directly or indirectly from person to person or a foetus *in utero* may acquire the disease from an infected mother. Certain animals may have the disease transmitted experimentally.

Syphilis is not a self-limiting infection for once the disease is present in the absence of treatment it will probably persist until the sufferer dies from that or any other cause.

The severity of the lesions in the absence of treatment varies enormously and in a few cases it even appears as if the disease burns itself out after many years so that no clinical or pathological test during life reveals any evidence of infection.

The incubation period is long usually about a month and by the time the first lesion has appeared the infection has been widely disseminated throughout the body. There is even experimental evidence that *S. pallida* can be found in the blood stream a few minutes after inoculation. This means that any prophylactic measures must be immediate if they are to be effective and shows how hopeless were the attempts in other days to abort the disease by excising the chancre.

It is impossible to forecast the course of the disease in any individual case but in general it is true that women are less severely affected than men and this is particularly so in late syphilis. No part of the body is safe from syphilis though there is a certain predilection for some organs and tissues.

It is customary arbitrarily to divide the course of acquired syphilis into certain stages. First there is an incubation period lasting from ten days to ten weeks and averaging about twenty five days during which there is no clinical evidence of disease. Then comes the primary stage of a local lesion

or lesions at the site of infection The local lesion is called the primary sore or chancre In the absence of treatment, signs of generalization varying greatly in extent and severity appear in about another four weeks, but may be seen sooner or even be delayed for some months. The primary sore may or may not be healed before this occurs

This is the secondary stage and it persists for about two years during which, if no treatment begins clinical signs may disappear and reappear The primary and secondary stages can be grouped together as early syphilis There follows the secondary stage, in most cases, a quiescent period in which the sufferer has no signs or symptoms Then comes the tertiary or late stage, usually beginning about three years after the original infection In the late stage the character of the disease has altered, the tissues having become allergic to *S pallida*, and their reactions are more indolent but more destructive. Lesions are more selective in distribution and are often confined to certain systems or organs

The special lesion of late syphilis is the gumma, which has the character of a chronic granuloma and which heals with much scarring Gummata may occur in any part of the body Besides the gumma, phenomena in late syphilis can be produced by vascular involvement resulting in diminution or cessation of blood supply to some part of the body for example, the brain or heart

The nervous system in late syphilis is liable to particular degenerative processes quite apart from any side effects from interference with its blood supply

The course of any case of untreated syphilis is liable to enormous variations The foregoing generalization applies to many cases, but sometimes the differentiation into stages is impossible, either because the lesions are so slight as to be unnoticed at one stage or because one stage merges imperceptibly into the next. The incubation period and the duration of the stages are also liable to be vastly different from the average.

The primary genital sore may appear at any time from ten days to ten weeks from the time of inoculation but there is some evidence to suggest that it is possible to have a genital infection without any chancre appearing In such a case the disease would appear directly in secondary manifestations

The primary stage is absent in cases where the infection is introduced by *blood transfusion* and there again the first signs are of the secondary variety Again, it is not uncommon for the primary sore to appear coincidentally with general manifestations The incubation period has been reported at less than ten days in cases of accidental infection of the buccal mucosa

The secondary stage may be very slight and fleeting and escape notice by the sufferer and may indeed be entirely absent Many patients with late syphilis can produce no history at all of any early lesions Rarely nowadays can still be seen extensive ulcerative secondary syphilis of a malignant type, resisting treatment and probably comparable with the original syphilis of the sixteenth century

The latent period of apparent good health between the secondary and tertiary stages is sometimes absent, secondary lesions, particularly of the skin persisting or fluctuating and gradually changing in their characteristics until a gummatous state is reached Skin lesions of an intermediate or secondo-tertiary type are described

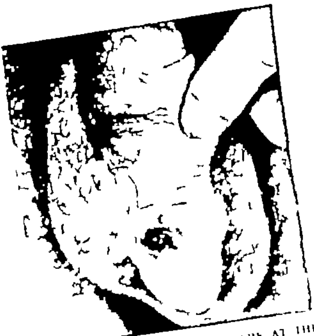
In other cases early inadequate treatment shortens the *period of latency* and precocious tertiary lesions have been seen as early as a year or eighteen months after original infection.

Although the earliest evidence of tertiary syphilis may be apparent in the average case in about three years the latent period for parenchymatous *neurosyphilis for example, tabes dorsalis* is generally much longer often 10 15 years or more after infection The same is true of cardiovascular syphilis

These and other visceral manifestations very often appear without any early tertiary manifestations, such as cutaneous or osseous gummata Indeed there is some evidence that those syphilitics who are affected in skin or bone with tertiary syphilis are less liable to neurosyphilis than those who escape A marked cutaneous secondary eruption is also to some extent a protector of the nervous system.

The cardiovascular system and other viscera do not appear to benefit so markedly from this protection

It is an error to imagine that neurosyphilitic manifestations are always late phenomena. The parenchymatous nervous lesions have a long incubation period but even here this may be reduced and the disease precipitated by early inadequate treatment.



ULCERATIVE SYPHILITIC CHANCRE AT THE FRENUM



EROSIVE SYPHILITIC CHANCRES OF THE LABIA

Signs of meningitic or meningo-vascular neurosyphilis may be evident as early as the secondary stage and many cases appear within 2–5 years of infection

In a surprisingly large number of cases latency after the early stages, even without treatment, may be lifelong and only a positive blood test remains to tell the tale. Even this evidence has been known to disappear after many years, though it is doubtful if the body ever succeeds unaided in entirely quelling the infection Manifestations of late syphilis rarely become clinically evident in acquired cases after the age of sixty

Congenital syphilis is comparable in its evolution to acquired syphilis There is, of course, no primary stage, the foetus being infected by the maternal blood as, by analogy in transfusion syphilis. The florid cutaneous lesions of infants compare with secondary lesions of the acquired disease and may be followed by a latent period before visceral involvement like that of late or tertiary syphilis. Here again there is infinite variety in the type of lesion and in the time of appearance. There is a further point of analogy in that the florid lesions of early congenital syphilis, like those of early acquired syphilis are heavily infected with *S pallida*, while the later manifestations are of the allergic type.

Syphilis has been well named the great imitator The cutaneous lesions of secondary syphilis can mimic many skin diseases In this connexion it appears as if syphilis, in a person liable to a particular skin disease, takes the guise of that disease in the secondary stage

Neurosyphilis, too particularly meningo-vascular and meningeal syphilis, can be confused with almost any nervous disease from cerebrospinal meningitis to disseminated sclerosis.

The prognosis in early syphilis with adequate treatment is good Regularity of treatment is much more important than the total dosage of drug, no matter what system of treatment is adopted and this fact must be forced upon the patient not once but every time he is seen

Relapse or recurrence of syphilis in an infectious form occur only in the first few years after infection Mucocutaneous relapse is the most important from the public health point of view but is easily treated. Much more dangerous to the actual patient is relapse involving the nervous system the eye or the heart.

Return of *infectious lesions can occur in untreated or* treated cases When a relapse is seen in a treated case, it is usually found that there has been inadequate or irregular treatment

Some patients are more prone to relapse or recurrence of infectious syphilis than others, and they are usually the ones who have had little *evidence of general reaction of the secondary* type immediately following the primary sore, and it is possible that a good secondary reaction particularly of the skin produces some tissue immunity protecting against relapse and recurrence.

The course of syphilis can be modified by many factors. The habits *of the sufferer have some bearing on the type of* secondary lesions. The less hygienic the more prone to moist condylomata lata. The coloured races show more variety than the white in types of cutaneous syphilides, but are less prone to parenchymatous neurosyphilis. This escape of the nervous system is particularly noticeable in the Moors and Arabs of North Africa.

Women resist syphilis much more than men and in this pregnancy seems to play an important part. Pregnancy seems to lessen the severity of the infection and to protect against visceral manifestations. Once visceral syphilis exists, however pregnancy may hasten its progress.

Poor general health alcoholism and starvation will all tend to increase the severity of syphilis at any stage Sunshine and abstinence from alcohol are thought to be factors in the scarcity of neurosyphilis in North Africa

THE SPREAD OF SYPHILIS

The vast majority of infections with syphilis are acquired by direct contact with an infected person Syphilis is transmissible in the primary and secondary stages particularly but it may also be spread by a person in the incubation period before any lesion has appeared The most infectious lesions of early syphilis are those in moist warm places hence the high incidence of primary sores on or about the genitals. Genital sore in a woman may result from transmission of *S pallida* in the semen of a male with early syphilis clinically evident or latent.

It has been said that *S pallida* cannot penetrate the unbroken skin, but enters through abrasions. Whether this is true or not, it is of no practical importance, as minute abrasions are nearly always to be found anywhere on the skin and sexual intercourse is bound to produce some even if the surface were previously intact In this connexion it is true that circumcized individuals are less liable to chancres on the glans than are the uncircumcized

A primary lesion generally appears at the site of inoculation. It may however be missed if it is small and fleeting or if it is concealed, as within the urethra The first evidence of disease would then seem to be secondary lesions It is possible that genuine cases can occur in which no chancre appears, and the disease is clinically generalized from the start. There is also syphilis d emblée in which the infection is directly introduced into the blood stream by the prick of a needle or by transfusion of fresh blood

GENITAL INFECTION

In civilized countries the vast majority of primary sores arise on or near the genitals the infection occurring during sexual intercourse, normal or perverted, with a partner having syphilis in the incubation period, the primary or secondary stage or relapsed secondary stage. A recent examination of a large series of case records showed that 97 per cent of primary sores were situated in the genital area — including thighs lower abdomen and anal region.

All observers agree that genital infection occurs in more than 90 per cent of cases.

EXTRAGENITAL INFECTION

Extragenital chancres can occur on any part of the body and have been seen by various observers everywhere between the scalp and the great toe. Here again, infection usually takes place during normal or abnormal sexual intercourse with a person in the early stages of syphilis

Chancres of the lips are the commonest of extragenital primary lesions, the infection usually being spread by kissing Primaries elsewhere in the mouth — tongue, tonsil palate,

gums, etc. — are less common Digital infection is also quite frequently seen and can result from titillation Doctors, particularly *obstetricians and ear nose and throat specialists who* work without gloves are sometimes the victims of physician's chancre Careless venereologists are not immune.

In handling lesions of early syphilis, the operator should always wear gloves or wash vigorously with soap and water for some minutes immediately afterwards It should be a rule that any intractable sore or whitlow on a doctor's hand must be suspect of syphilis until conclusively proved otherwise.

Chancre on the hand or knuckles can occur from striking an infected person on the mouth The eyelid may be infected by droplets coughed out by a person with secondaries in the mouth This again is a risk most commonly run by doctors The practice of removing foreign bodies from the conjunctival sac with the tongue has also been responsible for chancre of the eyelid The nipple is sometimes the site of a primary sore, and such infections were described in other days as occurring in wet nurses who suckled infants with congenital syphilis

Genital and extragenital chancres may co-exist in the same patient and cases with multiple extragenital chancres are sometimes seen

Extragenital infections are common in adults and children *in areas such as North Africa where syphilis is endemic.*

The diagnosis of syphilis is rarely made in cases of extragenital infection until signs of generalized syphilis appear These cases are a potential danger as is illustrated in the following instances

A surgeon with a digital chancre infected his wife The primary lesion appeared on the vulva, there having been a few small papules on the man's penis for a few days only His condition was diagnosed some weeks after the penile lesions had disappeared when secondary lesions of the buccal mucosa appeared He had been assured that the intractable whitlow was a low-grade infection

A man who afterwards developed a lip chancre had sexual intercourse with his fiancée about two weeks before his sore appeared He denied having had intercourse with any other women but admitted to *kissing a stranger The fiancée was* kept under observation Some nine weeks later she developed

a chancre of the vulva At no time did the man have any penile lesion, primary or secondary This was presumably an instance of transmission of *S pallida* in the semen.

MEDIATE INFECTION

Accidental infection is very rare, because *S pallida* is so easily destroyed by drying and exposure to the air There are however genuine cases of mediate transmission of infection by means of drinking glasses pipes, surgical instruments and so on

Sir Jonathan Hutchinson in his *Syphilis* gives some interesting examples, including cases occurring in children who had been vaccinated with material from other children with congenital syphilis, and instances where rabbis had spread infection while performing ritual circumcision In this latter instance the keeping of foreskins in the instrument case was presumed to be the important factor the original source having been an infant with congenital syphilis

HISTORY OF SYPHILIS

The word *syphilis* dates from the year 1530 when the famous poem, *Syphilis sive Morbus Gallicus* by Hieronymus Fracastorius was first published Syphilis did not at once become the universal name for the new disease described in the poem, and indeed it was not until the eighteenth century that it came into common usage

The disease we now know as syphilis was almost certainly introduced into Europe by the sailors of Columbus who had acquired it in Haiti on their return to Palos in 1493 General dissemination began in 1495 when the mercenary armies of Charles VIII of France entered Naples after a short siege. Alfonso II King of Naples, had been supplied with Spanish mercenaries by Ferdinand and Isabella of Spain. These soldiers, coming from Barcelona spread syphilis through Naples and the incoming armies of Charles VIII lost no time in acquiring the infection.

In 1495 it became necessary for Charles VIII to withdraw his troops into France where they were disbanded, and the soldiers went about the European continent spreading the disease.

Syphilis was first seen in England in 1496 in India in 1498 in Canton in 1505, in Japan in 1569, in Denmark in 1600 in Iceland in 1753 and in the Faroe Islands not until 1845

The new disease was first called by the name of the country from which it seemed to have been transported Thus the Spanish called *it the disease of Hispaniola, the French called* it the Spanish disease, and to the English it was known as the French disease. It was also known as the great pox, as distinct from the small pox or variola, and *lues venerea* or venereal plague, for its mode of spread was soon recognized

The first public health measures against syphilis were taken in Great Britain in April 1497 in Aberdeen where light women with the French disease were bidden to desist from their vices and sins of venery and were driven from their places of business

The spate of medical literature at the time leaves no doubt that the disease was new to the doctors and there is nothing to suggest that it was a modification or epidemic form of an already existing disease. The theory of the existence of syphilis in Europe before 1493 is also held, and its exponents quote from many classical sources in support The leprosy of Old Testament times is reputed really to have been syphilis. Extensive investigation of pre-Columbian skeletons in the Old World has provided no concrete evidence of the existence of osseous syphilis in this era Such evidence is however to be found in New World skeletons dating from before 1493 Osseous lesions were very prominent in the early days of European syphilis

Syphilis was at first a serious and mortal disease and its spread by accident and by venery was wide and rapid The severity of the disease declined rapidly with the passage of time This was forecast by Fracastorius. Now the fulminating and destructive syphilis of the early years is seldom seen in civilized countries although in North Africa a modified picture can be seen of what sixteenth-century Europeans must have looked like.

Gonorrhoea, or the clap was known long before syphilis appeared in Europe, yet a general controversy arose even within fifty years of the start of the epidemic as to whether the diseases were identical. In 1,67 John Hunter to settle the argument, inoculated his own penis with pus from

what he thought to be a straightforward case of gonorrhoea. He developed chancres and eventually died of the late effects of syphilis We now know that he must have chosen a case of mixed infection, but his experiment appeared to most people, though not to all, to finish the argument Only in 1837 was it conclusively proved by Ricord that the two diseases were distinct

The passage of syphilis to apes was first performed in 1903 by Metchnikoff and Roux, and the causative organism *S pallida*, was found in 1905 by Schaudinn. In 1906 the complement fixation reaction was applied by Wassermann and others to the diagnosis of syphilis, and a flocculation serum test followed in 1910, described by Jacobsthal

Nearly all the manifestations of syphilis had been accurately described a century ago but the final touch to the clinical description of the disease was added in 1913 when *S pallida* was found in the brains of general paretics by Noguchi, producing proof instead of conjecture that syphilis was indeed the basis of this condition

Mercury was used in the treatment of syphilis almost as soon as the disease appeared, and its use has continued until the present day No other drug of value was used until 1834 when William Wallace of Dublin introduced potassium iodide for the treatment of late secondary and tertiary lesions. Before this time guaiacum sarsaparilla and other drugs had their vogues but, naturally never supplanted mercury

No real advance in treatment came until about 1910 when Salvarsan, or 606 was prepared by Ehrlich who hoped that he had found the *therapia sterilisans magna* 606 was not the first arsenical preparation used in syphilis but it was the first relatively safe and effective one. Unfortunately the dream of a one-day cure for syphilis was not realized for though the results were spectacular they were not maintained. The drug was very toxic and difficult of preparation and administration so Ehrlich proceeded with his researches and produced 914 or Neosalvarsan This is the drug now most commonly used in the treatment of syphilis

It is not so potent as 606 but is more stable, less toxic and easier to administer In adequate doses and given regularly over a considerable period, it produced excellent results. 606 is still probably the best drug available for the treatment of

syphilis provided it is given in adequate doses but its dangers outweigh the therapeutic results, and as other drugs can safely though more slowly produce the same end result, it has largely been dropped from general use.

Bismuth was used in the treatment of syphilis as early as 1899, but not until the 1920's did its real value and proper application become established Arsenoxide was known to Ehrlich but its general use in the treatment of syphilis did not begin until about 1935 This drug is given in doses of about one-tenth the quantity of neo-arsphenamine and its therapeutic effects are reputed to be as good as those of 914 Arsenoxide is widely used in the United States, but has not yet found universal acceptance in Great Britain

The therapeutic value of malaria was made known in 1917 by Wagner von Jauregg and since then many advances in the production and use of fever in the treatment of syphilis have been made Since the time of Ehrlich the trend in treatment has always been towards reduction in the time necessary for a cure Satisfactory results in a fair percentage of cases have been obtained by massive arsenotherapy Massive or intensive treatment is discussed further on page 282 The application of this method is limited to special cases for the mortality rate is relatively high and the cure is by no means certain

CHAPTER XI

DIAGNOSIS OF SYPHILIS

SPIROCHAETA PALLIDA

Spirochaeta pallida, or *Treponema pallidum*, was discovered by Schaudinn in 1905. Schaudinn's discovery is remarkable in that it was made by direct microscopy before the dark-ground method of examination was perfected The spirochaete of syphilis is called *pallida* because it takes stains less than other spirochaetes *S pallida* is 0·25–0·5 μ in diameter and 4–24 μ long and has 6–24 spirals (Fig 11) The living organism, as seen by dark-ground examination moves slowly in the direction of its long axis and rotates in corkscrew fashion. Angulation at the centre occurs and the organism may even appear to knot itself, but the ends retain their rigidity and the coils remain regular Living *S pallida* can be found in specimens taken from the primary and secondary lesions of syphilis and examined by the dark-ground method, but never by this method in the cutaneous lesions of late syphilis

In specimens from genital lesions, *S pallida* is to be distinguished from *S refringens* and *S balanitidis* These latter are both gross organisms, thicker than *S pallida* and more loosely and irregularly coiled. They progress more quickly than *S pallida* and thrash about the field with sideways lashing movements. *S gracilis* also found in genital lesions, should cause no confusion as it is smaller much more slender and moves more rapidly than *S pallida* In mouth lesions, *S dentium* usually shorter and smaller than *S pallida*, may be confused but the slow purposeful movement of *S pallida* is diagnostic to the trained eye. *S pertenuis* the causative organism of yaws is indistinguishable in dark-ground examination from *S pallida*.

Staining methods for demonstrating *S pallida* in the secretions from early syphilitic lesions are available, but in clinical practice they are not admissible, for the only certain method of distinguishing *S pallida* from other spirochaetes is by the characteristic shape and movement seen in the living organism. *S pallida* has been demonstrated by various



FIG —SPIROCHAETA PALLIDA IN A DARK-GROUND PREPARATION

methods in all the tissues affected by syphilis and at all stages of the disease Culture of the organism is extremely difficult but is possible and reports have been made of transmission of the disease to animals by culture material Syphilitic lesions can be produced in certain animals by inoculation with infective material.

It has been suggested that S pallida is only one stage in the life-history of the causative organism of syphilis, but the postulators of this theory have not yet offered any concrete evidence in support Another unproved theory is that there are different strains of *S pallida* a dermotropic and a neurotropic This theory arises from the clinical observations that patients with severe cutaneous syphilis generally escape nervous complications. There is further clinical support for this idea in that there are well known instances of high incidence of neurosyphilis in patients who contracted the disease from one known donor

S pallida is present in large numbers in early syphilis in surface primary and secondary lesions, particularly in moist warm areas, and has been demonstrated in the blood cerebrospinal fluid and semen at the same stage. A negative Wassermann reaction is no criterion of safety for experimental evidence is available of the presence of *S pallida* in the circulating blood within a few minutes of primary inoculation, and transfusion syphilis has resulted from the use of blood from a sero-negative syphilitic In late syphilis five years or more after infection the persistence of *S pallida* in body fluids may be considered as very unlikely *S pallida* is soon destroyed by exposure to the air and by drying and is quickly killed by soap and water hence the rarity of chance infections apart from sexual contact

The pathological picture is essentially the same in all stages of syphilis The perivascular lymphatics are invaded and there is obliterative endarteritis with a perivascular

lymphocytic infiltration. Later plasma cells and fibroblasts appear and fibrosis and healing follow. Tissue destruction, a feature of late syphilis is not prominent in the early stages. The process varies in speed at the different stages of syphilis, being slower in evolution and in healing as the disease progresses. In early syphilis, *S. pallida* is easily demonstrable in large numbers in the lesions, but in gummata there are very few and prolonged search of serial sections may be necessary before an organism is found. The greater tissue reaction in extent in destructiveness and in duration in late syphilis is in indirect proportion to the numbers of infecting organisms present. This paradox is explained by the assumption that the body has become allergic and will produce a much greater reaction to the few remaining organisms.

It is an established fact that very often those patients who have a pronounced early reaction to syphilis with severe cutaneous secondary lesions escape clinical visceral damage. This was assumed by some observers in the past to mean that an immunity had been established and led them to delay treatment in early syphilis until secondary signs had appeared. This cannot be too strongly condemned on public health grounds, and there is no guarantee in any particular case that the infection will spare the deeper tissues while immunity is being built up. The presence of an acquired immunity in syphilis is demonstrated by the fact that after the appearance of the chancre, it is impossible to produce a super infection. This immunity rises through the secondary stage and gradually tails off, until in the late tertiary stage, it is possible for super infection to occur. This makes doubtful the old saying that the only test of cure for syphilis is to get another dose.

In the late allergic stage of syphilis, gummatous lesions have been artificially produced by the introduction of *S. pallida* into the tissues. This phenomenon led to the trial of cultures of *S. pallida* or material from heavily infected tissues for a cutaneous test in late syphilis. Unfortunately this reaction known as the Luetin test, has not proved specific.

BLOOD TESTS

The body reacts to an infection by *S. pallida* by producing an antibody and various laboratory methods have been

elaborated to demonstrate the presence or absence of this substance in the blood serum A threshold amount of antibody must be present in the blood serum before it becomes demonstrable in tests, and it is not essential to a diagnosis of syphilis to have a positive blood test. On the contrary the best prognosis can be given in cases where a diagnosis of syphilis is made on clinical signs and the finding of *S pallida* in the primary lesion before antibody titre has risen high enough to show a positive serological reaction

The Wassermann Reaction

This test for the presence of syphilitic antibody in the blood serum or in the cerebrospinal fluid is an elaboration of the Bordet-Gengou phenomenon of complement fixation A haemolytic system is used as an indicator to demonstrate the presence or absence of complement in a test antigen system

When sheep s red corpuscles are repeatedly injected into a rabbit the rabbit s blood serum comes in time to have the property of dissolving or haemolysing the foreign blood corpuscles If however the rabbit s serum is heated it loses this power of haemolysis, but can have it restored by the addition of any fresh blood serum such a that of a guinea pig

Three factors are involved in the reaction — antigen contained in the foreign blood corpuscles antibody which is formed as a response to the introduction of antigen in the recipient s blood serum and complement a universal factor present in all blood sera whi h is necessary to combine antigen and antibody together and omplete the system necessary to produce haem lysis This is known as a haemolytic system Antibody i more resistant to heating than is complement

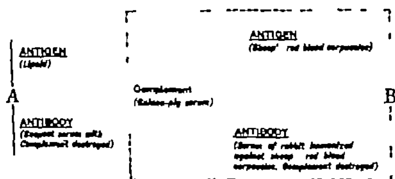
The intr du tion of an infecting organism such as *S pallida* into the human system also causes the production of an antibody and an antigen-antibody-complement linkage can take place The Wassermann reaction consists in the demonstration of this fixation of complement using a haemolytic system as an indicator and making use of the fact that complement is destroyed by heat

The syphilitic antigen first employed in the test was an extract of liver heavily infected with *S pallida* but it was later found that a non-specific lipoid antigen was ju t as effecti e

The antigen now used is a heart muscle extract with cholesterol

In the actual test the suspect blood serum is heated to destroy complement, is then diluted and mixed with antigen and has a measured amount of complement in the form of guinea pig serum added Time is allowed for any antibody antigen-complement linkage to take place and then the indicator—sensitized sheep's red corpuscles—is added The indicator consists of sheep's red cells with serum of rabbits immunized against them, but without complement. If the suspect serum contains syphilitic antibody then the added

THE WASSERMANN REACTION



A. Complement fixed by lipoid antigen and antibody in suspect serum. No haemolysis. Positive result.
B. Complement free to be fixed by indicator haemolytic system if there is no syphilitic antibody in suspect serum. Haemolysis. Negative result.

complement will be bound up with it and the syphilitic antigen. When the indicator is added no complement will be available to link up the haemolytic antigen and antibody and therefore no haemolysis will ensue. This is a positive result.

If there is no syphilitic antibody in the suspect serum, the added complement is free to complete the haemolytic system of the indicator and haemolysis occurs This is a negative result. The basis of the test is outlined diagrammatically

Many modifications are used in technique and in the material used as the syphilitic antigen and as the indicator The test is usually performed on several dilutions of the suspect serum and the results are stated as strongly positive (++) positive (+) and doubtful (±) If a doubtful result is returned then the test must be repeated on another sample of serum.

Flocculation Tests

These tests are antigen-antibody reactions comparable to the Wassermann test minus the indicator haemolytic system The antigen is non-specific Presence of antibody in the suspect serum is demonstrated by precipitation or flocculation which is visible to the naked eye and on microscopic examination Of many variations in technique, that of Kahn is most commonly used in Great Britain The results in this case are read directly from the test tube Of the tests employing microscopic examination Kline's slide test is best known

Use and Interpretation of Blood Tests

The results of blood tests especially in doubtful or latent cases must be viewed with caution Only tests performed by a recognized venereal disease pathologist should ever be accepted A solitary positive test in the absence of indisputable physical signs or other pathological evidence is not enough to convict At least two positive results must be returned in such a case before treatment starts and sometimes it may even be considered necessary to have the results controlled by sending a specimen to a second laboratory Complement fixation and flocculation tests are not mutually exclusive and whenever possible both should be employed

In early syphilis the Wassermann reaction often becomes positive before the Kahn test but occasionally the reverse occurs Generally in cases under treatment the Kahn test remains positive for a time after the Wassermann has reverted to negative

A pathologist will sometimes report that a serum is anticomplementary This means that it contains a substance which fixes complement and therefore inhibits haemolysis making the Wassermann reaction unreadable This occurs if serum is left standing for a long time or if the patient is suffering from some intercurrent disease Anti-complementary substances have no effect on flocculation tests

Blood tests become positive at or after the appearance of the chancre and in an untreated case by the time the chancre has been present from three to four weeks a positive result is to be expected in nearly 100 per cent of cases A negative blood test in early syphilis diagnosed by finding *S pallida*

means not that no immunity has been established, but only that the antibody has not yet reached the threshold value at which it is demonstrable by the existing tests.

In secondary syphilis, the blood tests are always positive, and persistently negative tests in a patient diagnosed clinically as secondary syphilis can only mean that the diagnosis is in correct. In latent syphilis and in the late stages of the disease with skin, bone, nervous or visceral involvement, blood tests are not invariably positive. There is a gradual diminution in positivity of the blood tests in untreated cases after the secondary stage, and eventually after many years some 20–30 per cent of such cases become sero-negative.

In congenital syphilis, blood tests are positive in the florid infantile type but may be negative in later stages. Persistently positive blood tests in an adult are evidence of syphilis even in the absence of clinical signs. Persistence of a doubtful reaction in an adult may mean either a congenital or an old latent acquired infection A meticulous clinical examination and a careful investigation of the family history including even the testing of other members of the family are indicated A very few individuals have a persistent doubtful reaction due to some unknown substance in the blood serum which is unrelated to syphilis A negative blood test is not positive proof of the absence of syphilis, for this can be found in the primary and in the late stages In certain diseases blood tests may be positive but revert to negative when the patient recovers. Among these are pneumonia, malaria glandular fever anaemias and acute infectious fevers Cases of yaws, a disease closely related to syphilis, give positive blood tests

For suspect latent syphilis with a doubtful or negative blood reaction, the provocative test with neo-arsphenamine can be used An intravenous injection of 0·3–0·45 gm. of neo-arsphenamine is given and the blood tests repeated in 5–7 days time. It is thought that in a case of syphilis the neo-arsphenamine, by its action on *S pallida*, stimulates antibody formation and so produces a positive or more strongly positive result. Under adequate treatment the reversal of a positive blood test in early syphilis is quickly accomplished and negativity will be maintained if treatment is continued

In late acquired syphilis and congenital syphilis reversal is more difficult and is sometimes impossible. In such cases the

length of treatment must be assessed on clinical progress and by the experience of the observer

From the foregoing observations, it is obvious that blood tests in syphilis must be considered as aids to diagnosis and treatment In some cases treatment will be given in the presence of a negative test in others treatment may be suspended although blood tests remain positive

THE CEREBROSPINAL FLUID

Examination of the cerebrospinal fluid is an important aid to the diagnosis of syphilis and in the estimation of progress and determination of cure. The technique of lumbar puncture is described on page 341

The following four tests performed on the cerebrospinal fluid are relevant in syphilis

(1) *Wassermann or Flocculation Test* The Wassermann reaction is generally used in Great Britain Anti-complementary and false positive reactions are very infrequent The test is strongly positive in nearly 100 per cent of cases of general paralysis of the insane and is positive in more than 50 per cent of tabetics. In early meningo-vascular syphilis the Wassermann reaction is often negative but becomes positive as the disease progresses

(2) *Cell Count* One to five lymphocytes per cubic millimetre is the normal range Six to ten cells per cubic millimetre is suspect and a count of over ten is abnormal. An increased cell count is evidence of a meningeal reaction and syphilis is one of a number of possible causes for this Predominantly meningeal syphilis is commonest in the earlier years of the disease and in such cases the cell count may rise into the hundreds

Parenchymatous neurosyphilis is usually associated with an abnormal cell count but on a lower scale between five and twenty cells per cubic millimetre A higher cell-count in such cases may be found in the early stages when a meningeal reaction is coincident

(3) *Globulin Estimation.* An increase in globulin content of the cerebrospinal fluid occurs in all types of meningitis including that due to syphilis The Nonne ammonium sulphate precipitation test is the one generally used

(4) *Lange's Test.* Changes in the content and state of globulin in the cerebrospinal fluid can be demonstrated by Lange's test. The fluid is added to colloidal gold solution, contained in ten test tubes, to produce a range of dilutions, and colour changes described in the numbers 0 to 5 are read off. A negative test reads 0000000000. In the absence of other changes in the fluid a result such as 0000121000 can also be read as negative. In neurosyphilis the readings vary in the different types. A high or paretic reading in the first zone or figures on the left is found in general paralysis of the insane, for example, 5555443210. In tabes and other types of neurosyphilis changes generally occur in the middle zone, or central figures, giving a so-called luetic reading, for example, 0012334210. High readings in the third zone are found in meningitic affections generally and are not specific in the diagnosis of syphilis. Tests similar to Lange's colloidal gold reaction can be done with colloidal benzoin or mastic and are read in a similar way.

Interpretation

The results of tests on the cerebrospinal fluid must be interpreted together. For example, a positive Wassermann reaction should be questioned if the other three tests give quite negative results in a patient without definite clinical evidence of disease. Again, a negative Wassermann reaction is not proof of absence of syphilis if a high cell-count and changes in the Lange test coincide.

The clinical state and the cerebrospinal fluid tests must be correlated. In a case of neurosyphilis, tests must be repeated at intervals although the time between tests need not be under months. This correlation of clinical and pathological findings is important in some cases in which it is possible for there to be an improvement in the pathological results while the clinical state worsens. Generally, however, a clinical recovery is accompanied by a corresponding pathological reversion towards normal.

The Wassermann reaction may be positive in the cerebrospinal fluid and negative in the blood. A high cell-count means a meningitic reaction and in most cases indicates that the prognosis with proper treatment is fairly good. Tests of the cerebrospinal fluid are most valuable, but unfortunately

are too infrequently performed This is, to a large extent due to the tales passed from patient to patient of the

THE CEREBROSPINAL FLUID IN NEUROSYPHILIS

		Cells per cub. mm.	Protein	Wassermann	Lange
Normal		0–5	15–30 mgm. per 100 c.c.	Negative	No change
Asymptomatic neurosyphilis	A	5–30	Normal or slight increase	Negative	N change
	B	0–100	Increased	Positive	N specific change
	C	0–400	Increased	Positive	5555543211 (paretic)
Acute syphilitic meningitis		Increased, up t 4000	Increased	Positive	Variable May be paretic or luetic
Meningo vascular syphilis		5 00	Increased	Positive	Variable Any change probably luetic
T bes dorsalis		0–100	Normal or increased	Negatn or positn (about 70% positi)	Variable negatn to 1234321 (luetic) or may be paretic
General paralysis of the insane		0–400	Increased	Positi	5555543210
Vascular neurosyphilis		0–50	Normal or increased	Negative or positive	N specific change

The hanges indicated here may be found during investigation or at routine lumbar puncture in patient under treatment or under observation. Types A and B would indicate treatment with one of the arsphenamine series, but type C requires the use of fever or tryparsamide or both

The blood W ssermann reaction in neurosyphilis bears no constant relation to the reaction in the cerebrospinal fluid but t is usual for positiv in the cerebrospinal fluid be paralleled in the blood I general paralysis of the insane the blood Wassermann reaction is positive in from 50 per cent of early cases to 99 per cent of late cases I tabes dorsalis the blood Wassermann reaction is positiv in 70 per cent, and in meningo-vascular syphil in bout 90 per cent of cases.

horrors of inexpert lumbar puncture If the patient can be convinced by a deft operator that the test is simple and causes little inconvenience, he can easily be persuaded to have the few repeated tests which give so much information as to progress in late syphilis and afford proper control in early cases

It must be remembered that neurosyphilis is not always a late phenomenon. There may be pathological and even clinical evidence of nervous system involvement even at the onset of syphilis and inadequate treatment can precipitate or pave the way for neurosyphilis. A properly controlled early case will therefore have at least one lumbar puncture during treatment, one at the completion of treatment, and one two years later when preliminary observation ceases. Only in this way can invasion of the nervous system be detected early enough to provide treatment which is likely to promote a rapid cure.

An indication for immediate treatment with fever and tryparsamide is what J H Stokes (*Modern Clinical Syphilology*) calls the red flag For example, Wassermann reaction strongly positive globulin increased cell count thirty-six per cubic millimetre Lange, 5555431000 Such a result in a treated or untreated case calls for heroic measures if the most serious involvement is to be avoided. The fact that the patient's clinical state may not correspond with the gravity of the findings in the cerebrospinal fluid must not be allowed to weigh against the use of intensive treatment.

Chapter XII

EARLY SYPHILIS

PRIMARY STAGE

The primary lesion or chancre appears at the site of inoculation after an incubation period of between ten days and ten weeks. Shorter and longer incubation periods have been noted in rare instances but the common time is 25–28 days

As already described the chancre may be so small as to be overlooked or in special instances of deep inoculation the primary stage may be omitted

The chancre generally begins as a small red macule which becomes a papule increases in size, and becomes eroded or ulcerated The further development of the chancre depends on the location treatment and presence or absence of secondary infection

A chancre or chancres may develop on what may be called prepared ground for example on a balanitis at the sites of herpetic lesions or on the burrows of scabies

In the absence of treatment the primary sore will eventually heal in anything from a few days to a few months, often leaving no signs Clinical evidence of a generalized infection may appear before or after the chancre has healed The primary lesion of syphilis is often solitary but multiple chancres are by no means rare occurring in 20–30 per cent of cases and multiplicity of lesions must not be thought to militate against a diagnosis of syphilis

GENITAL CHANCRES MALE

The majority of chancres occur on the prepuce coronal sulcus glans or frenum Sites next in frequency are the meatus the shaft of the penis and scrotum followed by the lower abdomen thighs and anus Intrameatal chancre infrequently occurs and is often missed entirely or diagnosed as a non-gonococcal urethritis if a urethral discharge is caused

Various types of primary sore can be described and the

classical Hunterian chancre is not the commonest The shape of the sore, for example serpiginous, crack or hour glass, can be used in description.


Fig. 12.—Erosive Syphilitic Chancre

Erosive Chancre

This is the commonest type seen (Figs. 12 and 13) It begins as a small red macule and becomes papular and eroded, and when fully developed varies in size from a pin head to about a quarter inch in diameter The eroded area is circular or oval in shape, has a sharp regular edge and a red granular moist surface. The edge is clearly defined and merges abruptly into the normal skin without any areola. There is no actual ulceration or extensive tissue destruction, and healing under treatment leaves no trace. Induration of the tissues under the chancre is minimal or absent. The appearance is as if a small


Fig 13.—Erosive Syphilitic Chancre
White patch is Elastoplast retractor



Fig. 14.—Ulcerative Chancre



Fig. 15.—Ulcerative Chancres



Fig. 6.—Ulcerative Chancre



Fig. 17.—Ulcerative Chancre with Destruction of Frenum



Fig. 8.—Hour-glass Type of Ulcerative Chancre



Fig 9.—Ulcerative Chancre



Fig 10.—Ulcerative Chancre

Fig 11.—Ulcerative Chancre of the Pub

area of surface epithelium had been cleanly shaved off with a sharp razor

Erosive chancres are generally seen when patients report early and it is probable that delay would cause a change in the appearance towards the ulcerative type



Fig 22.—Large Ulcerative Chancre of Lower Abdomen
Swellings on scrotum are sebaceous cysts

Ulcerative Chancre

This is the classical Hunterian, button or indurated chancre (Figs 14-22) The lesion is an oval or circular ulcer with a clearly defined edge, a surface of moist granulation tissue sometimes covered with a scab an indurated base and sometimes a faint pink areola fading into the surrounding skin Size is very variable On the lower abdomen ulcers as large as two inches in diameter have been seen



Fig. 23 —Papyraceous Chancre

The induration of the base can be felt as a button-like or cartilaginous mass when the sore is picked up between finger and thumb A subdivision of ulcerative chancre is papyraceous chancre (Fig 23) Here the ulcer is covered with a hard scab like brown paper but the general characteristics are the same. Ulcerative chancres may leave scars.

Chancre Oedema

Around ulcerative chancres there may be a



Fig 24.—Oedema with Ulcerative Chancre

certain amount of oedema, particularly when the lesion is on the prepuce (Fig 24) This oedema may sometimes be extensive and brawny Sometimes an area of oedema or induration with a darkening or brownish-red discoloration of the prepuce without actual erosion or ulceration is the primary lesion

Phagedenic Chancre

Secondary infection of a chancre with pyogenic organisms may produce widespread ulceration and gangrene of the prepuce, glans and shaft of the penis The ulcers have ragged bleeding edges are deep and have a sloughy base The surrounding skin is often black and oedematous *Spread* can occur over the scrotum and abdominal wall with great destruction of tissue and there is much scarring after healing

Mixed Chancre

It is not uncommon for a person to acquire a double infection with chancroid and syphilis. In such a case the original sore has the characteristic appearance of a soft sore and later when the incubation period of syphilis has been passed, changes towards the ulcerative chancre type (Fig 25)

Under sulphonamide treatment a chancroid may heal completely and the double infection be demonstrated after a lapse by the appearance on the same site of a syphilitic chancre.



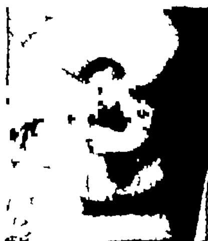
Fig 25.—Mixed Chancre
A double infection with syphilis and chancroid. The ulceration perforated the prepuce

Chancre with Phimosis

A syphilitic sore in a person with a tight prepuce is very apt to lead to irreducible phimosis Small crack ulcers may be seen round the preputial orifice, but often the sore or sores are completely concealed (Fig 26) A firm oedema of the prepuce is nearly always found. In such cases the feel of the inguinal glands is a great help in diagnosis for if this is suggestive of syphilis, it may be an indication for exposure of the under surface of the prepuce by dorsal slit. This operation should not be undertaken until gland puncture and a serological test for syphilis have been performed If either test confirms the diagnosis of syphilis there will probably be no need for operation because antisyphilis treatment in such cases is usually followed by rapid healing and the prepuce can soon be retracted again.

Meatal and Intra Urethral Chancre

Chancre at the external urinary meatus usually appears as a swelling or pouting of the lips of the orifice with redness, possibly erosion or ulceration and a serous discharge (Fig 27) The lips of the meatus are often sealed together


Fig 30.—Lip Chancre of the Erosive Type

Cervical chancres are usually of the erosive type and may simulate ordinary erosions if near the external os

Intra urethral chancre produces a pipe of induration which is palpable through the anterior vaginal wall Massive brawny chancre oedema sometimes occurs in the labia majora. Chancre of the vaginal wall itself is extremely rare. The characteristic inguinal glands are found with chancres of the external genitals but the satellite glands of cervical chancres are intra abdominal and cannot be felt

EXTRAGENITAL CHANCRES

Lips

Primary sores on the lips may resemble the erosive chancre common on the genitals (Fig 30) or they may be deeply ulcerated from secondary infection In general there is a tendency for lip chancres to be exuberant with much surrounding oedema


Fig 31 —Lip Chancre of the Exuberant Type



CIRCINATE AND CONDYLOMATOUS
SECONDARY SYPHILIS



VULVAL SYPHILITIC CHANCRE WITH
OEDEMA OF THE LABIUM

and prominent granulations (Fig 31) A painless swelling of the satellite lymph glands, submental or in the anterior triangle of the neck coincides The glandular enlargement is often massive and is unilateral as a rule (Fig 32)



Fig 32.—Lip Chancre with Marked Enlargement of Lymph Glands under the Jaw

Oral Cavity

Chancre on the tongue, gums or palate may be erosive or ulcerative in type usually the former If the tonsil is affected the lesion is often deep and ulcerative, covered with a thick slough, and easily confused with diphtheria or Vincent's angina.

Fingers

A true ulcer is sometimes seen on a finger (Fig 33) Usually the chancre simulates a whitlow or paronychia, and the sufferer presents himself with a secondary rash and a mutilated finger unhealed after one or more surgical operations. The satellite lymph gland may be epitrochlear or axillary depending on the finger affected

Eyelids

A small ulcer on the border of an eyelid or inner canthus is usually accompanied by marked oedema of the lid

DIAGNOSIS OF PRIMARY SYPHILIS

A certain diagnosis of syphilis in a case of genital sore is made only when pathological evidence confirms the clinical findings. In most cases dark-ground examination will disclose *S pallida* at once or after repeated tests. The technique of dark-ground examination is described on page 331 In the remainder a positive blood test at first or subsequent examination will give the necessary confirmatory evidence



Fig 33. [illegible] Scar of Groin

Any genital sore should be under suspicion until time and repeated tests have excluded syphilis

A suspect sore must have dark-ground examinations made upon its exudate until it is healed and blood tests must continue at regular *intervals until at least three* months have elapsed Only then if all tests have been negative may the suspicion of syphilis be dismissed Although certainty is only possible on pathological grounds, clinical findings will indicate the line of investigation The main conditions which may be confused with genital primary syphilis are considered separately

1 Chancroid

This is a condition which is easily confused with syphilitic chancre The important points in clinical differentiation are shown in the following table

	Primary syphilis	Chancroid
Incubation period	5 28 days	1 7 days
2. Number of sores	Often solitary	Often multiple
3. Shape	Circular or oval	Irregular
4. Edge	Sharp, clear-cut, little or no areola	Ragged, surrounding skin inflamed
5. Base	Red and granular with serous discharge	Dirty and sloughing
6. Local symptoms	None	Often tender
7 Inguinal glands	Typical painless discrete india-rubber glands	Tender inflamed and often suppurating
8. Dark-ground examination	*S pallida* present	*S pallida* not found
9. Blood tests	Positive (or negative at first, later positive)	Repeatedly negative
10. Sulphanilamide	No effect	Heals rapidly



HYPERTROPHIC SYPHILITIC CHANCRE
OF THE UPPER LIP



PAPULAR SECONDARY SYPHILIDE

PLA III

Pathological tests pertinent in the diagnosis of chancroid are described on page 300

2 Scabies

The penile lesions of scabies are large papules, possibly scabbed, but seldom truly ulcerated Multiple lesions are the rule. The typical scabies sites usually have burrows and itching is a prominent symptom. Any inguinal gland enlargement is unlike that in syphilis

3 Herpes Genitalis

In this condition a crop of minute vesicles appears first and gives way to pin point ulcers on the glans and inner surface of the prepuce. Inguinal glands are seldom enlarged The ulcers heal rapidly under treatment with saline washes and dusting powder Recurrence is common

4 Balanitis

Surface erosion is usually widespread on glans and inner surface of the prepuce. These cases must be carefully watched, for balanitis may be a forerunner of chancre

5 Traumatic Ulcer

Rupture of the frenum or cracking at the edge of the orifice of a tight prepuce generally occurs in sexual intercourse and is noticed at once. Routine observation and blood testing over three months will discover whether syphilis was contracted at the same time.

6 Carcinoma

Epithelioma of the penis is fortunately very rare It is usually an indolent ulcer with a hard rolled edge. The inguinal glands are hard and shotty Syphilitic chancre may be simulated If the condition is suspected a biopsy examination must not be delayed

The diagnosis of extragenital chancres is seldom made before clinical evidence of generalization is apparent Lip chancres have to be differentiated from herpes Vincent's angina, tuberculous sores gummata and from some rare fungus infections. The satellite glands may assist, but, as

always the final decision rests on the pathological findings

It is reasonable to suspect syphilis in the case of a chronic sore or whitlow in a medical man nurse or orderly

EXAMINATION OF A CASE SUSPECT OF EARLY SYPHILIS

A careful history is taken, including dates of all exposures suspect or otherwise, to infection, and the dates of onset of all signs and symptoms Notes are made of any previous attacks of venereal genito-urinary or skin disease, with details of treatment in the case of venereal disease. Details are taken of any treatment applied to lesions before reporting for examination

The patient should be examined stripped and in daylight if possible.

Any lesions of the skin and mucous membranes are noted the anal region not being forgotten Next the neck axillae, epitrochlear and inguinal regions are palpated to ascertain the condition of the lymphatic glands

Finally the genitals are particularly inspected and in women a speculum will be passed Any genital sores can be cleansed if necessary with saline solution.

Dark-ground examination of serum from a suspect lesion primary or secondary follows or serum is taken in a capillary tube for transmission to a pathologist

If *S pallida* is found the patient's general condition is assessed from the treatment angle, the urine is tested for albumen and the chosen drug or drugs administered Blood is collected for testing If an intravenous drug is to be used blood can be collected the syringe detached from the needle and another syringe containing the drug put in its place This obviates two separate venepunctures

The nature of syphilis the length of treatment and importance of regularity and general instructions are then explained. If possible all contacts (sexual) during the three months before the first signs should be examined and kept under observation

If at the first examination *S pallida* is not found the patient must attend daily for at least three days for dark ground tests

If lesions are very suspicious more than three tests will be

done, particularly if confirmation is not forthcoming in the blood test result.

The patient is warned to use only saline solution in cleansing any sores until a diagnosis has been made.

In the absence of positive findings, the patient is seen frequently until the sore has healed Blood tests should be repeated weekly in the first month fortnightly in the second month, and once at the end of the third month. Treatment may begin at any time if a positive result is returned and tallies with the clinical findings.

If all tests are negative over three months it is almost certain that syphilis can be excluded, but some workers advise that the period of observation should be for six months.

S pallida can be found in specimens of serum from primary and secondary syphilitic lesions In cases of difficulty as when a highly suspicious sore yields no *S pallida*, or where a sore is concealed by an irreducible phimosis puncture of an inguinal gland (see page 331) may hasten diagnosis

INSTRUCTIONS TO PATIENTS WITH SYPHILIS

When syphilis is diagnosed, it is important to discuss fully with the patient all aspects of the disease and explain the personal and public health obligations. The following fundamentals must not be omitted in cases of early syphilis

(1) Syphilis cannot be cured without treatment. If treatment is to be effective, it must be absolutely regular and continued until the physician in charge of the case is satisfied. Relapse and dangerous late manifestations are common only in the inadequately treated Prolonged observation is necessary after treatment ceases but the disheartening effect of this disclosure can be softened by explaining that this is for scientific interest.

(2) The disappearance of lesions or the negativity of blood tests do not mean that the disease is cured Generally twelve to eighteen months of actual treatment will be necessary

(3) Syphilis is infectious, but when treatment has started, the only danger to others lies in sexual intercourse. Coitus is not safe until a year after treatment has ceased and the patient has remained clinically and serologically negative in this time. Only in exceptional cases may coitus be resumed earlier and

then only after at least six months of treatment a condom being used

The patient must avoid kissing and nobody must use any article such as an eating utensil or pipe contaminated with his saliva Sufferers should sleep alone.

(4) Marriage, if contemplated should be delayed until a year has elapsed after treatment Women are advised that *pregnancy is unsafe for the same length of time* and that during any subsequent pregnancy they must have treatment as a precaution whether they have been pronounced cured or not

(5) Warning is given that any untoward symptoms or signs (for example vomiting skin eruptions etc.) occurring during treatment must immediately be reported

(6) The patient is told that if he is leaving the district at any time, *arrangements will be made for his treatment to* be continued wherever he goes

(7) Whenever possible the patient should be coerced into advising any possible contacts *that examination* and observation by a venereologist are necessary This is most important in marital cases where the other partner has been exposed to infection probably unwittingly before the first signs appeared In certain cases the patient may give details so that Regulation 33B may be employed

(8) Smoking should be suspended in the first few weeks of treatment particularly in secondary syphilis. Alcohol is *absolutely contra indicated throughout the course of treatment*

Chapter XIII

EARLY SYPHILIS (*continued*)

SECONDARY STAGE

Clinical evidence of generalization of infection is evident in the average untreated case in 3–6 weeks after the appearance of the chancre, or 7 10 weeks after inoculation. The chancre may still be present or it may have healed. The secondary stage may last 1–4 years, bursts of activity alternating with latent periods As time passes the signs of activity grow less and the latent periods longer The length of the secondary stage can be varied by individual and external factors, as can its manifestations

Inadequate early treatment may suppress the disease for a time, only to have a florid recurrence appear in weeks or months when the spirochaetes have multiplied and regained their vigour Again, a little treatment may shorten the secondary stage so that manifestations of late syphilis in skin or viscera appear earlier than usual the so-called precocious tertiarism Signs of the secondary stage may sometimes be fleeting or apparently entirely absent.

Whether signs are obvious or not the alteration of the character of syphilis from the early infective to the later allergic state is almost always complete by the end of four years.

The danger of an infected and untreated person to the community is greatest during the secondary stage, particularly during periods of clinical recurrences but decreases as time progresses.

All the tissues and organs are probably attacked by *S pallida* in the secondary stage, and a genuine upset of health is common just before and coincident with the first objective manifestations. The patient feels ill and weak and may have general joint and bone pains or headache. These general symptoms were a prominent feature of sixteenth-century syphilis. A low fever is not uncommon

According to the Co-operative Clinical Group in the United States, the various manifestations of secondary syphilis occur in the following proportions. Cutaneous syphilides 81 1 per

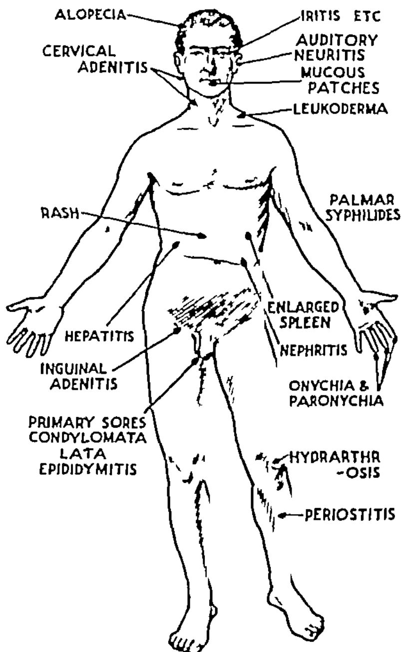


Fig 34—The Manifestations of Secondary Syphilis

cent, throat and mouth 36·5 per cent central nervous system 9·9 per cent, alopecia 7 1 per cent, ocular involvement 4 per cent, syphilis of other viscera 0·2 per cent.

The manifestations will be considered separately but for general purposes four cardinal signs of the secondary stage must be remembered

A. Cutaneous rashes	B Condylomata lata
C. Mucous patches	D General adenopathy

Any one or all of the many signs may be present in a particular instance, and, where recurrences take place in the fluctuating course of an untreated case, the manifestations may alter at different stages.

The Wassermann reaction and any other blood tests are positive in secondary syphilis Exceptions to this rule are so rare that it would be a brave man who would diagnose the condition in the face of a negative blood test, proved by repetition.

MANIFESTATIONS OF SECONDARY SYPHILIS

A. Cutaneous

Skin eruptions are a prominent feature of early and recurrent secondary syphilis. Early generalized rashes are usually situated on the chest, flanks, abdomen and flexor surfaces of the arms Except in the most florid cases, the face, scalp legs and backs of the arms are often spared.

Scaling is not very common and vesicles or bullae are exceedingly rare. Itching is usually absent, and is never severe. The lesions are usually oval or circular and are commonly reddish-brown in colour Distribution is bilateral and symmetrical. Almost any skin disease can be mimicked by secondary syphilis.

The types of rash encountered are macular papular pustular and ulcerative, with intermediate definitions of maculo-papular papulo-squamous and papulo-pustular A variety of lesions, macules, papules, etc. may co-exist in one case.

1 *Macular Syphilide*

The commonest early rash is the macular or roseolar syphilide. This consists of a diffuse mottling of the skin with

rose or ham-coloured macules, generally discrete oval or circular in shape, and varying in size from about one-eighth to a half inch in diameter No infiltration of the skin can be felt and pressure with a glass slide on the skin causes the lesions to blanch but not to disappear entirely

The rash may be very faint and only perceptible in good daylight. In such cases it quickly fades leaving no sign behind Other macular rashes are more obvious and may have a brownish or yellowish tinge. Such rashes last longer and may even leave for a short time some slight brownish pigmented remains.

The sites of election are the abdomen chest and fronts of the arms

Starting arsenical treatment may produce for forty-eight hours a transitory deepening in the colour so that the rash is more obvious before it begins quickly to fade This reactionary increase in the signs occurs with other types of rash

Differential Diagnosis Macular syphilides have to be distinguished from other eruptions Other evidence of syphilis will usually be found to substantiate any purely dermatological differentiation In measles there are fever conjunctivitis, Koplik's spots the rash affects the face, and the lesions coalesce

Streptococcal eruptions are accompanied by fever and by local evidence of infection in the tonsils or elsewhere.

In drug eruptions the rash is usually brighter and more scarlet than in syphilis and there is often confluence of the lesions The signs disappear on withdrawing the drug Sulphonamide rashes are liable to cause confusion particularly in an already suspect case of gonorrhoea

2 *Maculo-papular Syphilide*

About as frequent in incidence as the macular rash is the maculo-papular in which some of the lesions are infiltrated and slightly raised above the skin surface (Fig 35) The colour of the lesions is similar to that of a pure macular rash, but the eruption is more obvious Pigmentation persisting after the rash has faded is likelier than after a purely macular syphilide but is seldom pronounced

Differential Diagnosis An early pityriasis rosea may be confused with this type of syphilide but the tendency to scaling



Fig 15—Maculo-papular Syphilide

yellowish centre to the lesions, and herald patch of the former should help in diagnosis

3 *Papular Syphilide*

Less common than the macular or maculo-papular rashes papular syphilides are more widespread and accompanied by a greater disturbance in general health. The papules are



Fig 36.—Diffuse Papular Syphilide

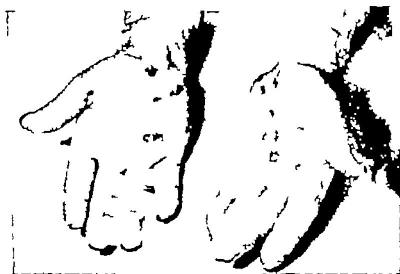
indurated and vary in size from a pin head to an orange pip Rarely papules as large as split peas are seen Usually all the papules are much the same size. They range in colour from yellowish brown to red Even in essentially papular eruptions some macules will be found (Figs 36 and 37)

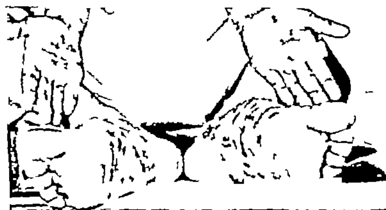
Papular syphilides quite often affect the face palms and soles Sometimes the hair margin of the forehead is picked out the so-called corona veneris Sometimes a little scaling is seen mostly at the edges of the papules and seldom a conspicuous feature This is the papulo-squamous type of eruption (Fig 38) There is some tendency for the lesions to be arranged in circular or serpiginous groups

Healing under treatment is slow and pigmented spots may remain for weeks or months but eventually disappear

Differential Diagnosis Small papular syphilides may be confused with lichen planus In this latter condition however itching is common the lesions are diamond or polygonal shaped flat-topped and purplish-coloured Acne should be distinguished by its duration and distribution on face chest and back, by the presence of blackheads and by the inflamed appearance of some of the lesions

Scabies is usually accompanied by intense itching worst





PAPULO-SQUAMOUS SECONDARY SYPHILIDES

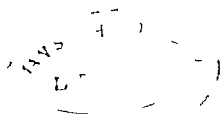




Fig 37 —Diffuse Papular Syphilis

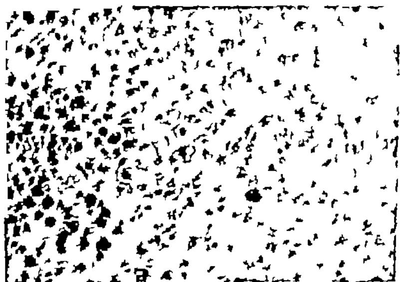
at night The lesions are widespread but typical burrows can usually be found about the hands and the *Sarcoptes scabiei* may be picked out and demonstrated Syphilis and scabies may and often do co-exist

Acute generalized psoriasis has usually marked scaling to distinguish it, and the lesions are likelier to attack extensor than flexor surfaces of the limbs. Psoriasis affects the scalp far oftener than does syphilis. In the rare case of syphilis in a subject of psoriasis the secondary lesions may adopt the form of the original disease and diagnosis will rest on other clinical and pathological evidence

Pityriasis rosea is distinguished by the herald patch central yellow colour and scaling of lesions, and by distribution along



Fig. 38 — Papulosquamous Syphilide.
Enlargement below shows scaling.



the lines of the ribs on the back.

Seborrhoeic dermatitis commonly affects the central back and chest the lesions are brownish, confluent and greasy and the scalp is usually involved.

4. *Pustular Syphilide*

A rare occurrence is the pure pustular eruption most cases being papulo-pustular where some of the papules have softened or ulcerated

The size and number of the pustules varies and in the most severe variety variola may be simulated—varioliform syphilide. Crusting may be marked as in the impetiginous syphilide, and in the most pronounced type, rupial syphilide (Fig 39) the scabs are hard and large like limpets. Ulceration is occasionally deep and destructive.

A rare syphilide is the framboesiform secondary marked by papular masses of friable purplish red granulation tissue In the same category is the corymbiform syphilide where large central papules are surrounded by satellites (Fig 40)

Pustular syphilides are widespread and often spare no part of the body This is the type of disease which was common in Columbian days and was then fatal in many cases. Though rarely now a mortal illness, the general malaise is very marked. the more so as already debilitated people are usually the victims.

Healing is slow and often followed by scarring where ulceration was deep

Differential Diagnosis Pustular acne will be diagnosed on long history and distribution. Variola is distinguished from the great pox by the more sudden onset, greater general disturbance of health fever distribution of lesions, etc

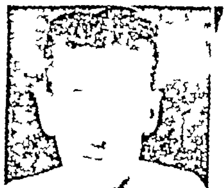
Impetigo or ecthyma may cause difficulty especially when widespread, for example when superimposed on a scabies.

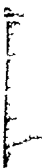
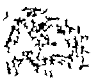
The diagnosis will finally rest in any case on the finding of *S pallida* in a primary or secondary lesion or on a positive blood test.

An experienced venereologist will, however begin treatment on making a certain clinical diagnosis of syphilis if delay is encountered in getting pathological results

5 *Recurrent Syphilides*

During the protracted course of an untreated syphilis,





Recurrent syphilides take the same forms as are found in early secondary syphilis (Fig 41) but on the whole they are apt to be more wide spread yet more discrete as regards the individual lesion. Recurrent roseolas are often a deeper red than the original type, and the papular syphilides frequently take ring or serpiginous shapes.



Fig 40.—Corymbiform Syphilide

Local cutaneous recurrence on the palms and soles is not uncommon The lesions are papular or papulo squamous, bilateral, and red or reddish-brown in colour Palmar syphilides are particularly liable to occur in manual workers

Recurrence on the skin of the genitals is usually of the variety of condylomata lata, but sometimes dry circinate papular lesions are seen (Figs. 42 and 43)



Fig. 41 —Discrete Lesion of Secondary Syphilis

The lesions of recurrent secondary syphilis are teeming with *spirochaetes which are* easily demonstrable, particularly from moist areas. The patients with small isolated recurrent lesions, particularly on the genitals are fruitful sources for the spread of infection

6 *Transitional Syphilides*

There are sometimes seen cases which do not correspond rigidly in clinical appearance with either secondary or tertiary syphilides These



FIG 4 —RECURRENT SYPHILIDE
Dry circinate lesions on the shaft. Primary sore has healed leaving phimosis and oedema of prepuce

secondo-tertiary cutaneous lesions are often localized and may be solitary or grouped Sometimes the lesions or groups of lesions are *bilateral* and *symmetrical* and this should always suggest syphilis Such distribution is not uncommon at the angles of the mouth Some hypertrophic lesions of the lips are also probably in the class of transitional syphilides

The transitional lesions are papular or nodular arranged in circular or serpiginous form with a tendency to radial spread Breakdown and ulceration are rare

Such lesion may be seen at any time from about two years





SECONDARY SYPHILITIC LESIONS OF BUCCAL MUCOUS MEMBRANE (MUCOUS PATCHES)

after infection onwards. The early appearance of transitional syphilides may be provoked by inadequate early treatment.

B *Condylomata Lata*

The appearance of cutaneous syphilitic lesions is modified by the nature of the soil. In moist places the manifestations are more exuberant. Condylomata lata—the surface lesions of moist areas—are reddish-brown or purplish, *flat topped*, *oval* or circular indurated papules. They are moist with serum which teems with *S pallida*. Condylomata lata are most commonly encountered with

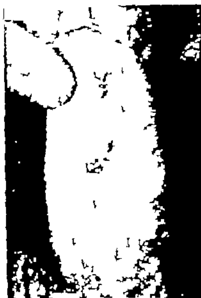


FIG 43—RECURRENT SYPHILIS ON MEDIAN RAPHE OF PENIS
These were the only lesions found

papular or pustular syphilides (Fig 44) but can occur as a solitary manifestation of the secondary stage. Lack of personal hygiene is a potent factor in the determination of their appearance.

In men condylomata lata occur on the glans and shaft of the penis, scrotum and anal region and upper inner sides of the thighs (Figs. 45 46 and 47)

In women the labia majora and perineal region are affected.

Less frequently condylomata lata may be found particularly in fat dirty people, in the inguinal folds, axillae or under pendulous breasts

Recurrent condylomatous lesions are often larger and fewer than those seen in the early secondary stage (Fig 48) Papules may reach half an inch in diameter and are exuberant and hypertrophic.

Similar moist papular lesions are also seen at the corners of the mouth and edge of the nose. Tissue hypertrophy particularly of the upper lip may occur in such cases especially when recurrent.



Fig 44—Condyloma Lata on Thigh and Shaft of Penis
A discrete papular syphilide is also present

The main point in differential diagnosis is from condylomata acuminata (Fig 49) These latter are rough and pedunculated with no discoverable *S pallida* in expressed serum The blood test result will be negative unless the patient also has syphilis.

Condylomata lata heal rapidly under arsenical treatment for syphilis ordinary warts are unaffected

C. Mucous Patches

The mucous membrane of the mouth is commonly affected usually coincident with a cutaneous secondary but sometimes alone. Recurrent attacks can be seen The inner surfaces of the lips fauces, tonsils, tongue cheeks, uvula and palate are possible sites

The typical mucous patch as commonly seen on the fauces is a very shallow erosive ulcer oval or circular in outline with a narrow pink or red edge and a base covered by a *thin white slimy membrane* which resembles in the classic description, a snail track. When the membrane is not present or if it is removed the base of the erosion is flat red granulation tissue

Lesions on the tongue are seldom covered by this white membrane and are often raised and papular Papular lesions can occur anywhere in the mouth

Coalescence of adjacent ulcers may give the whole a serpiginous edge



Fig 45 — Condyloma La on Shaft of Penis and Scrotum
A papular syphilide co-exists

There is often with or without actual mucous patches, an arc of reddening involving the faucial pillars, uvula and posterior edge of the soft palate. This circumscribed redness is unlike the general inflammation of the soft palate seen in heavy smokers

Deep ulceration occurs on the mucous patches when



The buccal lesions of secondary syphilis have to be distinguished from Vincent's angina, which may of course co-exist, from diphtheria, occasionally from gummatous ulcers, or from primary sore, particularly on the tonsil. Traumatic aphthous ulcers, the buccal lesions of erythema multiforme, and leukoplakia may also be confused.



Fig. 47.—Condyloma Latum on Shaft of Penis
Dorsal slit has been performed

D. Adenopathy

A general involvement of the lymphatic system of the body is common in secondary syphilis and may precede other signs or be the only sign. This is, of course, quite apart from the regional satellite glands associated with the primary sore.

The glands have the same firm india rubbery feel already described under primary syphilis. The inguinal glands, sub-occipital glands and those of the posterior triangle of the neck are oftenest palpable. Bilateral enlargement of the *epitrochlear glands is a sign pointing towards syphilis*, as is enlargement of the small post auricular glands lying on the mastoid processes.

The general adenopathy of syphilis has been confused with glandular fever and with Hodgkin's disease, but the blood test is always positive by the time this sign is apparent. There is a further risk of confusion in glandular fever in that the Wassermann reaction in this condition may give, for a time, a false positive result.

E. Leukoderma

This condition is sometimes seen in secondary syphilis and is commonest and most obvious in dark-haired women. It



Fig 48 Rect ent T re Condyloma Lat on Scrot

may follow a macular syphilide but is usually of independent origin The lesions are circular or oval macular areas of depigmentation with surrounding hyperpigmentation The spots are all about the same size Both sides of the neck and sometimes the shoulders are affected and a necklace effect can be produced Even under treatment it takes a year or two for the condition to fade Ultra violet light treatment may make the lesions less conspicuous

Erythema ab igne i differentiated by the f t that it i

usually unilateral and vitiligo by the finding of areas of depigmentation in other parts of the body

Leukoderma is a fairly late manifestation and its presence indicates that the disease has probably been present between six months and a year



FIG. 49.—CONDYLOMA A ACUMINATA A THE ANUS
This patient did not have syphilis

F Alopecia

Patchy falling of the hair particularly about the sides and back of the head is a phenomenon seen about six months or later after infection in some cases (Fig 50) The hair of the face, eyebrows and pubic region may be affected. It is allied to leukoderma and the two conditions often coincide. The end-result, which is easiest to see in men with close-cropped hair gives a moth-eaten appearance. The institution of treatment soon restores the hair

Examination of the cerebrospinal fluid in such cases very often gives evidence of an early meningeal reaction

Alopecia areata is differentiated by the fact that the patches here are clean-cut and often few in number while the syphilitic type is diffuse and the patches are not quite bald

A general falling of the hair is not uncommon in early secondary syphilis

G Onychia and Paronychia

Another manifestation of the later secondary stage, six months and more after infection, is affection of the nails Trauma plays some part in the development The condition is often multiple, a point of distinction from a primary whitlow chancre.

Nails may become furrowed and break off easily leaving a ragged edge, or fall off completely Paronychia runs a chronic



Fig 50. Marked Alopecia in Patient with Late Secondary Syphilis

course the tissues being swollen and dusky red There is seldom ulceration or pus formation and the condition is often painless unlike chronic whitlow due to septic infection

The pitted nails of psoriasis have to be distinguished and fungus infections will be diagnosed by finding the causative agent by microscopic examination of a nail shaving

11 Affections of Bones Joints etc

Osseous involvement in secondary syphilis common when

the disease was first seen in Europe, is now rarely encountered. Localized periostitis sometimes occurs, and the anterior surface of the tibia is a site of election, but any bone may be affected. A firm tender swelling is visible and palpable. Complete regression follows early treatment, but thickening of the bone may result if the diagnosis is missed.

Fleeting bone pains without any clinical evidence of involvement are sometimes a symptom. The bone pains are sometimes nocturnal, aggravated by heat and rest and relieved by movement.

Arthritis, hydrarthrosis, tenosynovitis, bursitis and myositis are seen in very rare instances.

I Hepatic Affections

A slight clinical jaundice with hepatic enlargement is occasionally seen in secondary syphilis and is generally associated with a florid eruption. Rarely is the jaundice deep. Jaundice and hepatitis may also be the result of early relapse of syphilis in the liver and may precede muco-cutaneous relapse.

Acute yellow atrophy has been described as occurring in untreated early syphilis, and if such a case were encountered, it would seem reasonable to try the effect of neo-arsphenamine or arsenoxide as an heroic measure in spite of the dangers. The liver in syphilis is fully considered on page 185.

J Kidney and Bladder Affections

Careful investigations of all cases would show that a small number of cases of early syphilis show some signs of renal involvement as demonstrated by a slight albuminuria, and by casts and red cells in the urine.

Acute nephritis of syphilitic origin is a very rare event which occurs in the early stages of the disease and is characterized by a very heavy albuminuria, oedema, anaemia and weakness. The treatment in such a case suspected, from collateral evidence, of being due to syphilis should be by neo-arsphenamine or arsenoxide in the first instance, because mercury or bismuth might aggravate the condition.

Macular and papular lesions of the bladder mucosa coincident with cutaneous secondary syphilis have been described.

K Affections of the Eyes

Clinically obvious involvement of the eye is rare in early syphilis Iritis can occur as a solitary phenomenon or as part of the syndrome of secondary syphilis. It is also seen as a sign of recurrence in untreated and in inadequately treated cases

The iris in such cases is irregular and there is circum corneal infection, but severe pain and gross inflammation of the eye are not common Haziness of the anterior chamber and keratitis punctata are also uncommon

Treatment apart from that of the syphilis which must be vigorous, consists of hot applications and keeping the iris well dilated with atropine. The results are usually very good in the early case.

Neuroretinitis has been reported as occurring in 11 1 per cent of a series of cases examined by the Co-operative Clinical Group. The condition seldom looked for and producing no symptoms in the patient clears up under treatment Inter stitial keratitis is an extreme rarity in acquired syphilis

L Auditory Affections

A syphilitic neuritis of the eighth nerve with tinnitus and diminution of hearing can occur in secondary syphilis. The effect of neo-arsphenamine in such cases is sometimes the production of a Herxheimer reaction which leaves the patient with an incurable deafness. If the auditory nerve is suspected of being involved treatment should start gently with iodides, mercury and bismuth

Vomiting and vertigo can result from early labyrinthine involvement

M Cardiovascular and Blood Affections

Clinically obvious affection of the cardiovascular system in early syphilis is rare Myocarditis and heatr block have been described *Early inadequate treatment has sometimes pro-voked* precocious tertiary lesions such as aneurysm within a year or two of infection True early lesions react well to treatment.

Moderate secondary anaemia is fairly common There may also be a leucocytosis to about 10 000 cells per cub mm with a relative and absolute lymphocytosis

N Affections of the Central Nervous System

S pallida has been recovered from the cerebrospinal fluid in cases of early syphilis even before any other pathological changes in the fluid were manifest

Abnormal findings in the fluid are astonishingly common According to the Co-operative Clinical Group, abnormal fluids were found in 28·3 per cent of cases of sero-negative primary syphilis, 29·8 per cent of cases of sero-positive primary syphilis, 34 1 per cent of cases of early secondary and 36 1 per cent of cases of late secondary syphilis

The patients with such findings rarely have clinical evidence of neurosyphilis and with adequate treatment are unlikely later to develop nervous disease.

Clinical neurosyphilis may be apparent at any time during the early course of the disease, but is usually delayed until a year or more after infection Meningeal and meningo-vascular affections predominate, but parenchymatous neurosyphilis can occur particularly as a recurrence after inadequate treatment

In only 1·7 per cent of cases studied by the Co-operative Clinical Group was clinical evidence of nervous involvement found in secondary syphilis

The types encountered may be

(1) *Basal Meningitis* When the meningitis is diffuse, there is headache, neck stiffness and retraction vomiting and all the signs of meningeal irritation and increased intracranial pressure

Localized meningitis produces signs and symptoms varying with the site affected. Various cranial nerves may be caught up in the process Facial palsy is the result of seventh nerve involvement. Diplopia and squint may result from interference with the third, fourth and sixth cranial nerves. The optic nerve may suffer in local or general meningitis, with resultant failure in vision. The eighth nerve already discussed or the fifth can also be affected

(2) *Diffuse Meningo-encephalitis* This results in mental and emotional changes and there may be coma and incontinence. Reflexes are increased, Babinski's sign is positive, and there may be pupil changes and local signs of involvement of particular cranial nerves.

(3) *Myelitis* The cord may be affected with urinary

retention, anaesthesia of lower limbs and later paralysis. Reflexes are increased in the early stages and abolished later The Brown-Séquard phenomenon may be produced

(4) *Mainly Vascular Syphilis* Hemiplegia may result from diminution or cessation of blood supply due to a syphilitic process involving the vessels supplying part of the brain particularly the internal capsule. Recurrent apoplectiform seizures may occur Epileptiform seizures can also be caused by vascular or meningeal involvement

The results of treatment in early neurosyphilis are quite good clinical and pathological regression occurring in the majority of cases

Miscellaneous

Besides the important signs in secondary syphilis discussed above, there are encountered many other inconstant phenomena such as fever headaches nausea anorexia with or apart from other stigmata.

The spleen is often enlarged and the thyroid gland may sometimes be swollen Epididymitis usually very mild and transient occurs rarely in secondary syphilis

RELAPSE IN EARLY SYPHILIS

Relapse or recurrence generally occurs within two years of infection or of cessation of treatment There appears to be a type of person particularly prone to relapse with or without treatment Relapse may be serological in that the blood test reverts to positive from negative or clinical when any of the manifestations of primary or secondary syphilis may reappear The lesions of a relapse secondary syphilis may be the same as the original early lesions or they may take another form Muco-cutaneous relapse has been described under the syphilides Neurological relapse may be clinical or pathological discovered only at routine testing of the cerebrospinal fluid Ocular osseous and hepatic relapses are all possible Evidence of relapse may also be given in the birth of a syphilitic child to an apparently healthy mother or when someone is infected by a person presenting no clinical or serological evidence of disease. In the latter case seminal infection may have occurred Reappearance of the chancre on its original site as a form of relapse is known as chancre redux Thus recurrent chancre

has all the characteristics of the original and is accompanied by satellite inguinal glands

S pallida can be found in the serum of chancre redux and in the glands Condylomata lata may mimic chancre redux and reactivation of a healed or healing chancre may take place as a secondary eruption appears Pseudo-chancre redux is a gummatous lesion on the site of the original chancre.

Muco-cutaneous relapse may occur during treatment, especially if this is irregular or intermittent. This is commonest in patients beginning treatment in the primary sero-negative stage, less frequent in primary sero-positive cases, and least in secondary cases. The development of cutaneous immunity probably explains this finding, which is paradoxical in that, with regular adequate treatment the sooner this is begun the better the prognosis in early syphilis Such relapses usually occur during a phase of treatment with a heavy metal alone.

Illustrative Cases

(1) A man with early secondary syphilis, roseola and adenopathy received two injections of neo-arsphenamine and then developed an erythema. This was erroneously considered to be an arsenical dermatitis and treatment continued regularly with bismuth injections weekly Ten weeks later a relapse papular syphilide appeared, accompanied by mucous patches and condylomata lata.

(2) A case of primary sero-negative syphilis was treated with eight weekly injections of neo-arsphenamine and bismuth, after which the patient defaulted He returned twelve weeks later with a mild jaundice and treatment began with bismuth only The jaundice deepened and two weeks later the chancre reappeared accompanied by a roseola and mucous patches. All the signs, including the jaundice, faded away rapidly when neo-arsphenamine was used.

Relapse can be reduced or entirely avoided only by careful treatment, which must be continuous, without rest periods and consist of an intravenous arsenical and intramuscular bismuth

The patient must be frequently examined for evidence of relapse and have blood tests at regular intervals The cerebro-spinal fluid should also be tested — routine, once in the early days of treatment, once at the end of treatment, and again at the end of preliminary observations

SYNOPSIS OF CHIEF SIGNS IN LATE SYPHILIS

1 Cutaneous gummata

2 Iritis, choroiditis, optic atrophy etc.

3 Gummata of submucous tissues and nasal bones.

4 Gummata of mouth pharynx and tongue Leukoplakia

5 Deafness from periostitis or eighth nerve involvement.

6 Gummata of muscles, including tongue and heart muscles.

7 Periostitis, osteitis, osteomyelitis, Charcot's joints, perforating ulcers of the feet

8. Bursitis tenosynovitis synovitis

9. Gummata of larynx and trachea. Gummata and interstitial fibrosis of lung

10 Gummata of viscera, liver spleen etc

11 Gumma or interstitial fibrosis of the testis

12 Cardiovascular syphilis — aortitis aneurysm etc.

13 Neurosyphilis meningeal vascular meningovascular gumma tabes dorsalis general paralysis of the insane

Chapter XIV

LATE SYPHILIS

SKIN AND MUCOUS MEMBRANES

If syphilis is adequately treated in the primary or secondary stages, the lesions heal rapidly and unless there has been deep ulceration leave no trace behind In the absence of treatment the tendency is usually towards the establishment of a balance between the infecting spirochaetes and the body's defences. In the first two or three years after infection relapses of various types may occur but eventually a state of latency is reached. The number of spirochaetes is greatly reduced by the natural defences and the method of tissue reaction changes. A state of allergy is established

This is known as the late or tertiary stage of syphilis and usually the change is complete by about four years after infection Whereas the lesions of early syphilis, original or relapse, are full of spirochaetes highly infectious and comparatively benign the lesions of late syphilis contain few spirochaetes, are non-infectious and may be, according to the situation, dangerous to the life of the sufferer

The time of appearance of lesions of late syphilis is very variable, and the latent period after the early stage may be non-existent or lifelong The secondary lesions may change imperceptibly to become transitional and then tertiary in character or inadequate treatment may speed up the clock so that precocious tertiary syphilis of any type can be seen in even less than a year after infection

In some cases no clinical evidence of late syphilis is ever apparent and even serological evidence may finally disappear There is autopsy evidence, however that a cure in syphilis with complete disappearance of all infecting organisms is probably impossible without treatment.

The important pathological lesion of late syphilis is the gumma Whether the process involves the skin bones or aorta, the underlying pathology is the same. The gumma is a granuloma produced by the allergic reaction of the tissue to the spirochaetes. This allergic change is responsible for the



Fig 51 —Solitary Gummatous Ulcer of the Forearm

exaggerated response to a comparatively small number of spirochaetes. There is infiltration of the tissues round the organism with lymphocytes plasma cells and epithelioid cells The small vessels in the area suffer an obliterative endarteritis, blood supply is reduced or abolished and central necrosis ensues.

The end-result is similar to that seen in tuberculosis, save that tissue destruction is seldom so marked Giant cells are also seen This basic process is the same in all the lesions no matter what the size

CUTANEOUS GUMMATA

Any part of the body surface may be affected in late syphilis, and there is no special site of election Gummata may be solitary or multiple and vary enormously in size They are often grouped and never so numerous or diffuse as secondary lesions

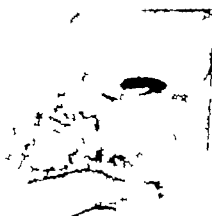


Fig 52 —Solitary Gumma [illegible] of Lip

The types encountered are nodular nodulo-ulcerative and ulcerative. Cutaneous gummata may appear at any time from a few years to a decade and more after infection.

The classical gumma begins as a firm reddish-brown nodule in the skin. This nodule softens centrally breaks down and an ulcer is formed

The ulcerative gumma is often solitary and may vary in size from about a quarter of an inch to several inches in diameter (Figs. 51 and 52) Oval or circular in shape, the ulcer has a deep sharp edge and a punched-out appearance. There is a tendency to spread at the edges, and there is often a brown or bluish areola of induration The base of the ulcer may at first be covered with a yellow wash-leather slough. Very deep ulcers may discover the tendons or muscles (Figs. 53 and 54) There is usually no associated pain or tenderness. Two or more ulcers side by side may fuse in their growth, producing one large serpiginous ulcer

Healing can take place with or without treatment, and a thin scar and local pigmentation are left. The scar is often very poor and breaks down easily with slight trauma. There is some reason to believe that gummata may be precipitated at a particular spot by local trauma.

Nodular gummata are generally multiple and arranged in groups (Fig 55) If more than one group is formed, asymmetry is the rule, unlike early syphilis The nodules are small, up to about the size of a split pea, and reddish-brown They are arranged in circles or arcs (Fig 56)

Always in late syphilis there is a tendency to centrifugal spread, and new nodules form at the outside of the circles, with healing in the centre. The healing may take place with or without scarring Very often there is little scar but pigmentation is common (Fig 57) Coalescence of two growing arcs or circles may produce curious gyrate or serpiginous forms, and in the protracted course of the disease very large areas may in time be covered.

Scaling is quite a common feature of nodular gummata, especially on the palms and soles (Fig. 58)

The nodulo-ulcerative type is very much the same as the pure nodular Some of the lesions go on to ulceration, but spread is the same. The ulceration is seldom so deep or extensive as with solitary gummata, but healing leaves

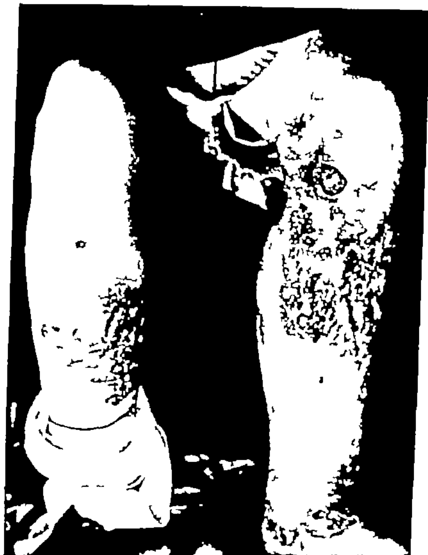


FIG 53 — MULTIPLE DEEP GUMMATOUS ULCERS OF LEGS

more scar than after the nodular type (Figs. 59 and 60)

Differential Diagnosis

Ulcerative gumma of the leg can be confused with varicose ulcer In the latter varicose veins are usually obvious eczema is often a precursor and the ulcer is more likely to be solitary The Wassermann reaction is usually positive with



Fig. 54.—Gummatous Ulceration of Legs penetrating as deep as the Muscles

gummata but may be positive even with a varicose ulcer if syphilis coincides. In dubious cases rapid healing under anti syphilitic treatment will clinch the diagnosis.

Cutaneous tuberculides sometimes may resemble gummata, but the Wassermann reaction or a therapeutic test in special cases will usually differentiate the two conditions. Mycotic infections of the hands and face can be excluded by finding the causal agent in pus or tissues Carcinoma cutis can be excluded by biopsy if it is suspect.



Fig 55. Nodular Gumma of the Back
An early case

Nodular gummata have to be distinguished from psoriasis (particularly on the hands and feet) and sarcoid

Solitary gummata on the lip may ape a chancre as may late recurrence on the penis pseudo-chancre redux

In all cases of doubt the Wassermann reaction, therapeutic test and biopsy are at the disposal of the clinician


Fig. 56.—Spreading Circinate Nodular Gummata of Neck

Careful history-taking is, of course, a first essential The Wassermann reaction result will usually be enough, though it must be remembered that a small percentage of cases of late cutaneous syphilis have a negative reaction. For this small group the other two tests will be used In taking specimens for biopsy a deep wedge of tissue, including some normal skin is removed under local anaesthesia.

The following case illustrates the procedure in a difficult case. A man aged twenty four had a chronic recurrent ulceration of the dorsum of one foot This was thought to be gummatous, and anti-syphilitic treatment was started when the Wassermann reaction was found to be repeatedly positive No improvement was apparent, and a biopsy was performed when the condition was proved to be tuberculous. The latent syphilis was purely coincidental


Fig. 57—Pigmentation at the Edge of Healing Nodular Gumma of the Arm

THE MOUTH AND TONGUE

Gumma of the soft palate begins as a firm painless swelling followed by ulceration which may destroy the whole of the tissue including the uvula The tonsils and fauces are sometimes included in the process. A tonsil alone may



Fig 58.—Gummata of the Soles

be the site of a gumma Any such pharyngeal ulceration causes voice changes and possibly dysphagia but pain is seldom prominent Destruction is often very rapid and healing under treatment is accompanied by much scarring

Gummatous ulceration of the hard palate is primarily periosteal or osseous and perforation of the palate is fairly common This

Fig 59.—Nodulo-ulcerative Gumma of the Back

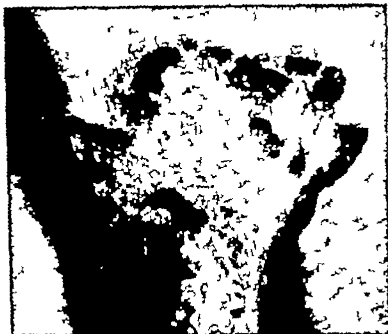


Fig 60.—Nodulo-ulcerative Gumma of the Palate

may be accompanied by intra nasal destruction The process is again painless and in some cases may never be noticed until nasal regurgitation of fluids occurs. Gumma of the palate is nearly always in the midline

Palatal and pharyngeal gummata have to be distinguished from Vincent's angina and from carcinoma both of which may in rare cases proceed even as far as perforation. The gums are often affected in Vincent's infection. In a suspect case, if the blood test is negative and Vincent's organisms are not found a biopsy will be necessary

The tongue may be the site of a gumma or gummata. Solitary gumma begins as a painless swelling in the tongue, which may finally break down to form an ulcer

Gummatous infiltration of the tongue produces a hardening and fibrosis of the organ giving it a lobulated appearance. The mobility is affected in any case and speech may be altered

Leukoplakia (Fig 61) is very commonly due to late syphilis, combined with a mechanical factor such as smoking or bad teeth. The inner surfaces of the cheeks at the angles of the mouth and the surface of the tongue are most commonly affected



Fig 6 —Advanced Leukoplakia

but any part of the buccal mucosa may suffer

It is thought that leukoplakia is developed on the site of mucosal secondary lesions Leukoplakia is the end scarring of a superficial syphilitic glossitis, and is usually a fairly late phenomenon often delayed ten years or more after infection

In the early stages the tongue or cheeks show smooth red glazed oval or circular patches As time goes on the surface of these areas becomes scarred and white, the typical leukoplakia

The condition is important in that it may be a stepping stone to carcinoma of tongue or buccal mucosa Transition stages are seen when the leukoplakic patches begin to crack and ulcerate Treatment does not give spectacular results

Certain cases of recurrent papular mucosal syphilis of the tongue resemble closely an early chronic superficial glossitis Complete and rapid disappearance of lesions under treatment will show that the early stage has not passed

Gummatous ulcers on the tongue lips and corners of the mouth have to be distinguished from tuberculosis and carcinoma The history complete physical examination, blood tests and if necessary biopsy will establish a diagnosis

A leukoplakic condition of the vulva or of the inner surface of the prepuce can occur late in tertiary syphilis

Chapter XV

LATE SYPHILIS (*continued*)

THE VISCERA

THE LIVER IN SYPHILIS

Hepatic involvement of various types may occur at any stage of congenital or acquired syphilis during and apart from treatment.

Congenital Syphilis

In early congenital syphilis a diffuse pericellular fibrosis with enlargement of the liver is common The spleen is also enlarged Jaundice is rare. *S pallida* abounds in the livers of early congenital syphilitics Late in the course of the disease gummata may arise and produce symptoms of jaundice or ascites, the cases resembling types seen in late acquired syphilis Intercurrent hepatitis is encountered during the course of treatment of congenital syphilitics with the arsenicals This is identical with the hepatitis seen in treated acquired syphilitics. It is very rare in children, but is common in adults

Acquired Syphilis

Early

A mild hepatitis has long been noted as occurring in early syphilis before treatment begins Clinical jaundice is rare, occurring in about 0 1–1·0 per cent of cases. Jaundice usually coincides with a severe florid secondary syphilis. A symptomless hepatitis which resolves under treatment is probably commoner

Recurrence of early syphilis in the liver manifested in hepatitis and jaundice, is also encountered. These cases are no different from the type seen in untreated syphilis and may precede a muco-cutaneous recurrence

Biopsy by liver puncture in one case of jaundice in early syphilis showed a moderate hepatitis with periportal infiltration and some centrilobular collapse, the whole picture indistinguishable from that seen in material from cases of jaundice

occurring as an incident during arsenical treatment No evidence of hepatitis was found at biopsy in a case of secondary syphilis showing no clinical signs of liver damage.

All these cases, primary or recurrent clear up quickly on arsenical treatment though there may be an initial reactionary deepening of the jaundice after the first treatment

Acute yellow atrophy has been noted in very rare cases as occurring in untreated early syphilis

Late

Clinically obvious hepatic syphilis is not common in the late stages, and post mortem examinations are not demonstrative of a very marked incidence of latent affections.

Gummata of the liver are always multiple, ranging in size from the minute to large palpable tumours. Breakdown is followed by fibrosis, and contraction of scar tissue distorts the liver producing an end state of hepar lobatum Irregular low fever is common with liver gummata Other symptoms depend on the situation of the tumours, but jaundice ascites, or both can occur Splenic enlargement commonly occurs with hepatic syphilis

Diffuse interstitial fibrosis and perihepatitis are also seen singly or together The symptoms include jaundice ascites, fever and abdominal pain like that of cholelithiasis The whole picture is like that of ordinary cirrhosis

The results of treatment are variable for if there is much fibrosis there may be chronic ascites or jaundice and oesophageal varices may be formed

In differential diagnosis gall bladder disease ordinary cirrhosis and secondary deposits of carcinoma are to be considered Associated splenic enlargement and a positive blood test will be signs for a therapeutic test Mercury will be used at first Bismuth has to be used with caution in late hepatic syphilis and arsenic entirely avoided

Hepatitis associated with Treatment

Jaundice during the course of the arsenical treatment is fairly common, occurring in about 5 per cent of cases in normal times. There are encountered four main types of hepatitis of which the first two are by far the commonest

(*a*) Acute mild hepatitis (clinical and sub-clinical)
(*b*) Chronic and more severe hepatitis
(*c*) Subacute yellow atrophy
(*d*) Acute yellow atrophy

Acute mild hepatitis manifests itself with indigestion, nausea, vomiting and anorexia followed by jaundice. The urine is dark and the stools may be pale. Joint pains and urticaria are also found as prodromal symptoms in some cases. The liver is slightly enlarged and the spleen may be palpable. Urobilinogen may be found in excess in the urine for some days or weeks before clinical signs appear Abortive cases, in which the gastric symptoms are not followed by clinical jaundice, are quite common.

When symptoms or the appearance of urobilinogen or bile in the urine suggest that hepatitis is starting arsenical treatment should be suspended or reduced while bismuth continues. In this way some cases may be aborted. Most acute cases recover in anything from a few days to two or three weeks.

Chronic hepatitis begins in the same way but runs a more protracted course, lasting up to two or three months. The liver is larger symptoms are more severe, wasting is pronounced and the depth of the jaundice is fluctuant. Eventual clinical recovery is the rule, but pathological examination at a later date may show some slight scarring

Subacute yellow atrophy is rare. The onset is the same as in the less severe cases but after a week or two the patient becomes very ill There are two types one in which ascites is prominent, one where cholaemic symptoms accompany a deep jaundice. The majority recover but there is evidence of severe liver damage with coarse cirrhosis in biopsy material from such cases.

Acute yellow atrophy is fortunately rare. From beginnings as already described the patient rapidly passes into cholaemia and dies in a few days or weeks. It is often impossible in the early days to decide, in any given case, what will be the out come — a mild hepatitis or an acute atrophy

There is no clinical or pathological evidence to distinguish such cases from non-syphilitic persons with infective hepatitis The pathological picture is, in the early stages of diffuse hepatitis with round-cell infiltration and degeneration of the parenchymal cells This state may be followed by complete

recovery as in the mild cases, or may be progressive to a state of acute liver atrophy

In the chronic cases there is progress from the original picture described above, towards a zonal hepatitis central or periportal with proliferation of bile-ducts and some fibrosis The end result here is either complete recovery or a slight degree of fibrosis insufficient to cause trouble In subacute liver atrophy a severe zonal hepatitis is followed by gross fibrosis which cannot completely resolve. Representative sections made from biopsy specimens are shown in Fig 61

Jaundice during neo-arsphenamine treatment occurs usually at the time of the eleventh to the fifteenth injection or from the fifteenth to twentieth week after treatment begins The time of onset is about the same with Mapharside. Jaundice has also been noted during bismuth treatment with original arsphenamine with massive arsenotherapy and was described by Hutchinson in the days of mercury

The incidence varies considerably and parallels the infective hepatitis rate in the healthy population but at a much higher figure

Reduction in certain constituents of the diet is a possible factor for the incidence rose to a peak in 1920 after the war of 1914–18 in 1930 during the slump and is markedly rising again since 1940

Above a certain point increasing the dosage of an arsphenamine preparation produces more cases of jaundice and reducing greatly the dose of arsenic by the use of Mapharside lowers the rate The incidence of jaundice during treatment is negligible in women and young children

It may be reasonably concluded that the jaundice coincident with arsenical treatment is the same as infective hepatitis, but that syphilitics are for a number of reasons much more prone to succumb The factors which may be involved in the production of hepatitis are (*a*) arsenic (*b*) dietary deficiency (*c*) syphilis itself (*d*) environment, for example, overcrowding (*e*) sex, (*f*) virus infection.

Mode of Action of Arsenicals in Relation to Liver Damage

Whipple and others have shown that the detoxication of poisons such as chloroform carbon tetrachloride arsphenamine etc., can be accomplished by the liver on a high protein

diet. If protein is deficient the addition of amino-acids containing sulphur in a sulphydryl group such as methionine, cysteine, or cystine with choline, will enable detoxication to proceed satisfactorily

Such sulphydryl amino-acids are necessary for the life of the cell and if too much is used in processes of detoxication the vital processes of the liver cells will suffer

Glutathione, present in the liver cells, is responsible for the carriage of oxygen and hydrogen and for detoxication This substance contains in its molecule three amino-acids one of which, cysteine, contains the sulphydryl group

The work of Eagle has shown that the lethal action of the arsphenamines is due to their oxidation in the body to arsenoxide which combines with the glutathione of the spirochaetes and arrests their internal metabolism.

Arsenoxide introduced directly or indirectly as an arsphenamine, is lethal to the spirochaetes, but also to the liver cells if their sulphydryl content is low

The maintenance of a high concentration of sulphydryls in the liver might make it possible to protect against damage by arsenicals. This procedure would also be theoretically liable to protect the spirochaete by rapidly detoxicating the arsenoxide.

Arsenoxide introduced directly in small doses has probably lost its spirochaeticidal effect in a few hours. The arsphenamines slowly oxidized to arsenoxide, remain actively spirochaeticidal for longer periods. The toxic effect of the arsphenamines is much greater than arsenoxide because much more arsenic is employed and in practice the incidence of jaundice is about three times as great with neo-arsphenamine as with Mapharside in single weekly doses On theoretical grounds arsenoxide should be given at more frequent intervals than neo-arsphenamine and practice has confirmed this.

It is clear that the action of arsenicals is closely related to the production of liver damage, but it is obvious that other factors are involved because the incidence fluctuates Infection can deplete liver sulphur reserves and a virus infection superimposed on damaged liver cells is probably concerned in most, if not all, cases

Diet reductions in war time affect particularly the staples containing sulphydryl groups—milk, cheese and eggs In this

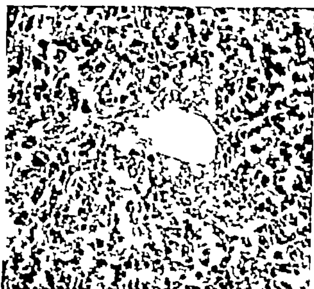


Fig 6 A.—Biopsy Specimen obtained by Liver Puncture

Diffuse hepatitis with fragmentation of liver cell columns and histiocytic and round cell proliferation. From patient with hepatitis during arsenical treatment for syphilis. Clinical cure a month later

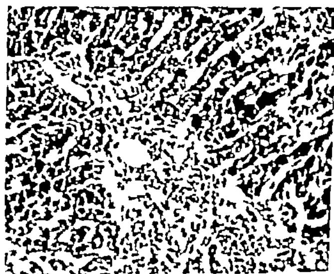


Fig 6 Biopsy Specimen

Peri-portal and central zonal damage with bile duct proliferation and new cellular connective tissue From patient with hepatitis during arsenical treatment for syphilis. Clinical cure month later



Fig 6 a.—Biopsy Specimen

Zonal scarring in central and peri-portal regions. From case of relapsing hepatitis after arsenical treatment for syphilis

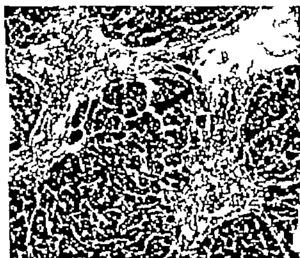


Fig. 6 b.—Biopsy Specimen

Classical cirrhosis with nodular areas of liver cells, and new bile duct formation in the fibrous tissue. Specimen taken four months after severe hepatitis with ascites in patient undergoing arsenical treatment for syphilis

connexion it is notable that jaundice, common enough in hospital practice, is almost unknown in the well-fed private patient in peace-time.

The existence of an infective factor probably virus, has been proved by transmission experiments in human volunteers who developed hepatitis after inoculation with blood serum from patients with post-arsphenamine jaundice The disease is probably the same as the hepatitis produced by transfusion of blood from donors with latent hepatitis and that which followed inoculation with certain batches of yellow fever vaccine diluted with human serum In all such cases the incubation period is around eighty days. By taking the utmost care to avoid any passage of infective material in syringes, particularly by adequate sterilization by boiling or autoclaving the incidence of hepatitis can be kept very low

To sum up the important factors involved in hepatitis during arsenical treatment are arsenic, sulphydryl deficiency and infection, and prophylaxis lies in proper sterilization of syringes between patients and provision of a high protein diet.

Early Recognition of Liver Damage

As has already been related clinical icterus is sometimes preceded by certain prodromal symptoms such as indigestion nausea, joint pains or urticaria. The excretion of urobilinogen in the urine is also increased at this time and a simple test is available for the estimation of this substance This test should be performed routine if possible when the urine is being tested for the presence of albumen before each treatment.

5 c c of freshly passed urine in a test tube is cooled by holding the tube under the cold tap for one minute To this is added 2 3 drops of a 2 per cent solution of paradimethyl aminobenzaldehyde in 5 per cent hydrochloric acid A definite pink or red colour developing at once indicates an excess of urobilinogen

If impending liver complications are suspected particularly at the critical period between the fifteenth and twentieth weeks of arsenical treatment arsenical injections should be temporarily suspended for a week or two Bismuth treatment must of course continue. In this way a certain number of patients may be saved from proceeding to established icterus

GASTRO-INTESTINAL TRACT

Syphilitic lesions of the stomach and intestines are very rare indeed, but gummata have been described as occurring at all levels.

The oesophagus can be the site of a submucous gumma which may produce dysphagia during the active stage, or may later *if fibrosis occurs, produce a constriction* In the stomach solitary or multiple gummata and a diffuse gummatous submucous infiltration have been noted This last type of lesion produces a condition of leather bottle stomach similar to that seen in diffuse carcinoma.

Diagnosis in such cases is made on a basis of other clinical evidence of syphilis pathological findings and particularly on the results of therapeutic trial

Local gummata or diffuse gummatous infiltration are also said to occur in the small intestine and rectum. Ulcerative lesions of the rectum, anus and perineum may occur but in young people such a condition is more likely to be due to lymphogranuloma inguinale. The Frei test will usually decide the issue, and should not be omitted even if the Wassermann reaction is positive. Carcinoma must also be excluded

GENITO-URINARY TRACT

Gummata, solitary or diffuse of the kidney bladder prostate gland and of the uterus or other female pelvic organs are extremely rare Ulceration in the bladder may be a cause of haematuria Bladder function may be indirectly affected in neurosyphilis.

TESTIS

The testis can be the site of a solitary gumma, or it may be permeated by diffuse gummatous infiltration with interstitial fibrosis This latter condition is sometimes bilateral.

Gumma produces a slow painless enlargement of the testis which may become as large as an orange (Fig 62) Hydrocele is sometimes associated and ulceration through the overlying skin on the antero-lateral surface of the scrotum can occur

Diffuse interstitial fibrosis causes a hard swelling of the testis, seldom very large, but quite insensitive, so that the organ can be squeezed without any protest from the patient. Hydrocele sometimes coincides but ulceration of the skin is never seen Late syphilis of the testicle may draw attention by the swelling



FIG 61.—BILATERAL GUMMATA OF TESTES
This patient was operated for hydrocele He also had syphilitic aortic incompetence

or it may be found on routine examination in association with other evidence of the disease

The epididymis is very rarely involved and the vas deferens and seminal vesicles are unaffected This helps to differentiate tuberculosis or gonococcal epididymitis. Sinus formation is likely with tuberculosis but ulceration is rare Swelling due to any form of epididymitis is more rapid than in syphilis of the testicle pain is a feature and sensation is not lost

Malignant disease of the testis produces a hard swelling with loss of sensation, but the enlargement is progressive and often rapid Regional lymphatic involvement is common

Ultimate diagnosis rests in pathological findings and therapeutic trial, but this latter must not be over long if there is any question of malignancy

Treatment gives good results in arresting the process but restoration of actual function is unlikely

THE EYE

Cutaneous gummatous lesions occur on the eyelids and occasionally may spread to affect the conjunctiva. Interstitial keratitis, so common in congenital syphilis is one of the greatest rarities in acquired syphilis. Gumma, behind the globe, in the orbital cavity can be a cause of unilateral proptosis, which has to be distinguished from malignant disease of the orbit.

Iritis, choroiditis and retinitis are also occasional occurrences in late syphilis

Paralyses of the external ocular muscles are due to intracranial affection of the nerves

The lachrymal glands alone or with the salivary glands, may be enlarged, one form of Mikulicz syndrome

Primary optic atrophy is an important complication It may occur alone or more commonly with tabes dorsalis. Visual failure may progress to complete blindness. Central scotoma and reduction of the peripheral fields is found. Ophthalmoscopy shows pallor of the disc. Secondary optic atrophy can follow a choroido-retinitis.

The results of treatment are not very good in primary atrophy a little better in the secondary type.

THE EAR

The external ear can be involved in a cutaneous gumma, and periostitis also can occur on the bony parts. The function of hearing can be affected in late nervous syphilis

RESPIRATORY SYSTEM

Larynx

Gummatous changes on the larynx are fairly common and result in hoarseness of the voice and sometimes in aphonia. There may be ulceration. The condition has to be distinguished from tuberculosis and from malignant disease. Haemorrhage, common with cancer is rare in syphilis. Signs in the chest will usually be found with a tuberculous laryngitis. The Wassermann reaction and therapeutic trial will aid diagnosis. In instituting treatment the arsenicals must not be employed,

for their too early use can precipitate a local oedema which may prove fatal Oedema of the glottis apart from treatment is rare. Hoarseness may persist or even become more pronounced after treatment as a result of scarring

The trachea and bronchi are very rarely affected but gummata have been described as occurring there Symptoms here include inspiratory stridor brassy cough and paroxysmal asthmatic attacks

Lungs and Pleura

Late syphilis may affect the lungs with a solitary gumma diffuse fibrosis and possibly a broncho-pneumonia

The signs and radiological appearances may suggest chronic tuberculosis or malignancy Collateral evidence of syphilis will suggest a trial of anti-syphilis therapy in suspect cases. Arsenic will not be used as the danger of reaction is too great If a lung condition is indeed syphilitic the results of treatment are rapid and good Secondary pleural affection can occur in such cases

Cases of delayed resolution when lobar pneumonia complicates syphilis have been described and are said to react quickly to antisyphilis treatment

J H Stokes (*Modern Clinical Syphilology*) considers that although pulmonary syphilis is clinically obscure it is probably not very rare. Authentic pulmonary syphilis is not uncommon in North Africa the syphilologist s paradise

ENDOCRINE GLANDS

Thyroid

A diffuse sclerosis may produce woody hardness of the thyroid Hyper or hypo-thyroidism can be associated A gumma may become adherent to the skin and even ulcerate. Dyspnoea is a result of tracheal pressure Carcinoma is to be excluded in differential diagnosis

Pancreas

An interstitial fibrosis and a gummatous pancreatitis have been described A syphilitic diabetes can be produced, and this reacts to antisyphilis treatment even without dietetic measures.

Adrenal Glands

The symptoms of Addison's disease can in rare instances, be produced by a late syphilitic involvement of the adrenals

Pituitary Gland

Simmond's disease, a premature senility due to hypopituitarism may be caused by syphilis Gumma of the pituitary has been discovered in some such cases.

MUSCLES, BONES AND JOINTS

The Muscles

Late syphilis of muscles is rare, but may take the form of a diffuse myositis or a gumma. Gumma may spread and produce ulceration of the overlying skin

The tongue, as already described, is a fairly common location for gumma, and very rarely a small gumma in the myocardium may cause heart block from interference with the conductive system.

The Bones

Late osseous syphilis is relatively common, and is believed to offer some protection against nervous and cardiovascular involvement. The skull, long bones and shoulder girdle are most liable to attack.

Periostitis is the most frequent lesion and the inner third of the clavicle, tibia or ribs are often picked out. Local or diffuse lesions are seen In the early stages the swelling is tender to pressure, but this sign becomes less as time goes on The bone is irregularly thickened and the added tissue may become ossified Necrosis and ulceration of the overlying skin can also occur

Osteomyelitis less common than periostitis, can again be local or diffuse The symptoms are like those of pyogenic osteomyelitis but less severe and more prolonged. There is local pain and tenderness with possibly some swelling The cranial bones are often affected (Fig 63) Necrosis and sequestration of bone occurs (Fig 64)

Gummatous processes affecting the periosteum, bone and cartilage of the nose can be very destructive. The septum may



Fig 65.—Osseous Syphilis involving the Bones of the Nose and Palate

be perforated or completely destroyed and the bridge of the nose flattened (Fig 65) This may be accompanied by cutaneous gummata of the face or occur alone. There is a foul purulent discharge from the nose. This condition has to be distinguished from lupus Blood tests, therapeutic trial and biopsy will help in diagnosis. The hard palate may be perforated by a gummatous osteoperiostitis

Ostitis is the rarest of the bone lesions In the diffuse type there is great thickening and sclerosis of the cortex, shown dense on X ray photographs (Fig 66) Local cortical gummata produce central necrosis with sequestrum formation around which is an areola of dense sclerosis. The small bones of the hands and feet may be affected by a syphilitic dactylitis. The main points in diagnosis are tuberculosis and sarcoma



Fig 64.—Mutilating Osseous and Cutaneous Syphilis



Fig 65.—Osseous and Visceral Syphilis

Left, tumour of parotid gland ; *Right*, results of Radium treatment. Saddle nose concealed by plaster Original investigation did not include blood test for syphilis and cutaneous gummata appeared after treatment of the tumour

differentiated by radiological appearance, blood test results and trial of therapy

JOINTS, TENDON SHEATHS AND BURSAE

Rarely extension of a gummatous process in bone may affect a large joint, spreading into the synovial membrane. Swelling and hydrarthrosis are unaccompanied by pain, and mobility is little affected Tendon sheaths can also be affected by a gummatous infiltration.

Bursitis is also rare. The prepatellar bursae are the usual location, the walls being infiltrated by gumma (Fig 67) The condition is commonly bilateral and ulceration through the skin can occur

Charcot s Joint

This condition is not directly due to syphilis and can occur quite apart from it, as in syringomyelia (Fig 68)

In tabes dorsalis changes in the large joints knee, ankle, hip, shoulder elbow etc., of a hypertrophic osteo-arthritic type can occur Interference with the innervation of the joint, particularly appreciation of pain, is the precipitating factor



Fig. [illegible] S[illegible] Chr[illegible]
All [illegible] from [illegible]

It is possible that spontaneous unrecognized fracture involving the joint is a forerunner

A swollen crepitating but painless joint is the result. At first, free movement is apparent but later the growth of osteophytes and destruction of the articular surfaces may cause restriction. Sometimes after the initial great hydrarthrosis a flail joint is the result capsule and ligaments having been stretched and weakened. X-ray pictures show great destruction of the bones, with areas of hypertrophy rarefaction and loose bodies. (Figs 69, 70, 71)



Fig 67.—Gummata of Prepatellar Bursa

The joint is classically described as feeling like a bag of bones. The absence of pain in spite of gross physical signs is a point in diagnosis. Other evidence of tabes dorsalis will usually be present.



Fig 68.—Charcot's Joint

THE CARDIOVASCULAR SYSTEM

Syphilis is essentially a vascular disease in all its stages. The aorta and the arterioles are mainly affected, the intermediate arteries rarely suffering sufficiently to give rise to clinical signs. The myocardium can be affected in a number of ways, directly and indirectly. Venous syphilis occurs in the late stages as a


Fig 69.—Charcot's Joint (Elbow)

phlebitis affecting the saphenous or superficial arm veins.

The vascular changes, arteritis and endarteritis, underlie the necrosis in gummata the hemiplegia when the blood system of the internal capsule is involved angina pectoris and indeed most of the manifestations of syphilis.

Syphilis is responsible for some 10 15 per cent of all cases of cardiovascular disease, and this type of syphilis is the cause of death in about 30 per cent of persons dying as a direct result of the disease. Women are affected much less often than men

Cardiovascular syphilis is seldom recognized clinically until between ten and thirty years after infection Aortic aneurysm and other phenomena have appeared as precocious tertiary lesions occurring even less than a year after infection in inadequately treated cases So common and important is this complication that no follow up of a treated case or examination of a latent syphilitic is complete without radiological investigation of the heart and aorta.

Heart and Coronary Arteries

The rarest cardiac lesion is the discrete gumma of the myocardium, which may produce heart block if located on the course of the conducting bundles

Secondary myocardial fibrosis occurs when a coronary vessel is occluded True coronary involvement is much rarer than narrowing or occlusion of the mouths of the vessels by an aortitis. The result may be angina pectoris or coronary



Fig 70.—Charcot's Joint (Knee)

thrombosis, and either condition in a young person should provoke an investigation for signs of syphilis.

A chronic syphilitic myocarditis can occur alone or with an aortitis. Secondary degenerative changes are seen in the myocardium in cases of aortic incompetence.

Cases of sudden death, due apparently to an acute syphilitic myocarditis have been described by Warthin. Here over exertion and heat were precipitating causes, and were followed by dyspnoea, cyanosis, palpitation and collapse. *S pallida* was found in the heart muscle of all the cases described

Pericarditis is rare in syphilis and accompanies a myocardial lesion.

The Aorta

The pathological process is a lymphatic spread periaortitis and a mesaortitis due to an involvement of the vasa vasorum

symptoms may of course, co-exist Death may occur in an anginal attack or from heart failure due to decompensation

The signs and symptoms produced by aneurysm vary naturally according to its situation There is usually cardiac enlargement, and coincident signs of aortic incompetence or angina or both are not infrequent Evidence of pressure of the tumour on the trachea great veins vertebral column or bronchus may be found Severe pain accompanies erosion of bone by an aneurysm. An abnormal area of dulness co-extensive with the cardiac dulness may be found on percussion and occasionally a palpable pulsating tumour is evident. The pulses may be asynchronous and the blood pressure different on the two sides. Aortic dilatation is evident radiologically and pulsation can be seen on fluoroscopic examination. Death may be caused by rupture of the aneurysm or by heart failure

Peripheral Vessels

Aneurysmal dilatations can occur in the smaller arteries The femoral popliteal and cerebral vessels particularly the circle of Willis, are affected

Endarteritis of cerebral vessels produces a variety of nervous lesions, the type depending on the site of the disease Obliterative endarteritis of the arteries of the legs and feet can produce gangrene of the toes and intermittent claudication Ayerza's disease may be due to syphilis of the pulmonary arteries in some cases.

Prognosis If treatment begins before signs of myocardial degeneration are evident an arrest of the process may be attained and a fairly good prognosis given

Dilatation of the heart and anginal symptoms are very unfavourable points Arrest of progress in established aneurysm is rare Treatment must always begin gently and arsenic has no place in the early stages.

CHAPTER XVI

LATE SYPHILIS (*continued*)

THE NERVOUS SYSTEM

NEUROSYPHILIS is a fairly frequent and most important complication. Predisposition to attack is induced by the inadequate use of the arsenicals but there is no basis for the statement, made in the past, that there has been an increase in the neurosyphilis rate generally since arsenicals were used

Those affected by marked cutaneous lesions early or late, or by osseous syphilis, are least liable to nervous affections. In North Africa neurosyphilis is very rare in the native population. The factors involved in this instance include a high incidence of cutaneous and osseous syphilis, a very low rate of alcoholism, and abundant sunshine. The few recorded cases of general paralysis have all occurred in alcoholics or in individuals who had become Europeanized Kraft Ebing has summarized the situation in his dictum that neurosyphilis requires syphilization and civilization Males are more prone to neurosyphilis than females. In the case of general paralysis the proportion is 9 2

The aim in practice should be to treat syphilis early and adequately and to diagnose nervous involvement early when it is still in a stage where treatment can be effective. This will be accomplished by a technique of full and frequent clinical examination, and by the acquisition of skill in lumbar puncture so that patients will not default from the repeated tests necessary in a properly controlled course of treatment.

The prognosis in all types of nervous syphilis is, with modern treatment constantly improving, and some change for the better can be confidently expected in nearly all cases.

Meningeal and vascular neurosyphilis of the early stages have already been discussed In late syphilis the main types of involvement have been classified by Stokes as

1 Meningeal and meningo-vasculo-parenchymatous.
2 Predominantly vascular
3. Predominantly parenchymato-meningo-vascular

Brain Gumma and Encephalitis

A *solitary gumma* can produce all the signs and symptoms associated with any cerebral tumour In some cases where pathological tests are negative a therapeutic test will be necessary to help in establishing the diagnosis If the pituitary is the site of a gumma, a variety of syndromes may result including Simmonds's disease and diabetes insipidus.

Multiple gummata produce symptoms like those of meningeal syphilis or of the rare diffuse syphilitic encephalitis In this latter condition coma and delirium are followed by signs of ocular and peripheral palsies An acute form is fatal but recovery with residual psychic changes can occur in subacute or chronic cases

General Paralysis of the Insane

The pathological picture in this type of cerebral syphilis varies enormously from case to case, and the clinical appearances follow suit Findings of pure parenchymatous affection of the brain are rare vascular and meningeal lesions occurring in almost every case and producing symptoms and signs which may predominate

The main pathological changes include a diffuse inflammatory reaction in the cerebrum particularly about the vessels and meninges perivascular cellular infiltration and parenchymal degeneration with gliosis (Fig 73) There is wasting of the brain flattening of the sulci and dilation of the ventricles.

The Wassermann reaction in the blood is positive in nearly 100 per cent of cases. In the cerebrospinal fluid the Wassermann reaction is strongly positive globulin is increased the cell count is increased and the Lange test gives a paretic or high first zone reading Serological findings of this kind can be encountered before clinical evidence is apparent the condition being often termed paresis sine paresi

Such findings whether found alone or with clinical signs of neurosyphilis are an indication for urgent and drastic treatment.

General paralysis of the insane is usually found in the second and later decades after infection The typical clinical picture may be *preceded or accompanied by* or punctuated

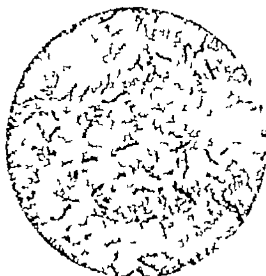


Fig. 73.—Spirochaeta Pallida in Brain Tissue from a Case of General Paralysis of the Insane

with signs of meningeal or vascular neurosyphilis. A series of apoplectic attacks may occur during the course of the disease or there may be ocular palsies or other evidence of meningitis The condition of taboparesis is one in which the main features are those of tabes dorsalis, but are accompanied by signs of general paralysis of the insane of secondary importance.

The commonest type of general paralysis of the insane is characterized by simple dementia with gradual progression to amentia. There is an excited type with mania and delusions of grandeur and a depressed type melancholic and suicidal. Rarest of all is the rapid progressive type where a series of epileptiform attacks occur in quick succession each attack leaving the patient weaker mentally and physically than the last, until death occurs in a convulsive state

General Symptomatology The early symptoms are often headache, insomnia, irritability and forgetfulness. The patient s friends will notice character changes, carelessness, lack of judgment, moral laxity Delusions of grandeur or wealth may appear or there may be depression Epileptiform or apoplectic attacks may occur the latter followed by paralyses which tend to recover

Pupillary changes are always present and usually marked The *Argyll Robertson* effect of reaction to accommodation but not to light is frequent Irregularity and inequality of size are frequently seen Optic atrophy may be found The face is flat and vacuous and there is often tremor of the facial muscles and tongue. The speech is hesitating slurred and indistinct and syllables may be dropped Writing is shaky and words or syllables are omitted The legs are weak and the gait unsteady Tendon reflexes are generally exaggerated except in taboparesis and in the late stages when they are absent. The plantar response may be flexor or extensor There is a spastic paresis of the legs and control of the bladder and rectal sphincters may be lost

In the late stages paralysis and contractures are seen and the patient becomes bedridden Death occurs from exhaustion or intercurrent infection

The course is run in three to five years in the average case, but a few go rapidly in three to six months, while others drag on as long as twenty years.

Remissions occur in some untreated cases and the sufferers return to a state of normality for a time usually six to twelve months, before relapsing

A good recovery under treatment can be obtained in early cases, but if the disease is arrested late the patient may have slipped far down the intellectual scale

THE SPINAL CORD

The spinal cord is liable to the same types of pathological lesions as the brain and spinal and cerebral neurosyphilis often co-exist Sensory disturbances are commoner than motor for the lesions are predominantly in the posterior parts of the cord including the meninges sensory horns and posterior and lateral columns

Vascular Syphilis

Thrombosis of the anterior spinal artery has an apoplecti form onset with complete flaccid paralysis of trunk, arms and legs. Spasticity follows.

Spinal Meningomyelitis

The early symptoms are pain in the neck or back and

bladder control disturbance. Paraesthesias and pains in the limbs with hyperaesthesia at the painful points also occur

There is weakness of the legs with spasticity increased reflexes and extensor plantar response

Diminution in sensation or even anaesthesia below the level of the lesion may be found. Progress of the disease results in loss of reflexes and flaccid paralysis. The Wassermann reaction in blood and cerebrospinal fluid is positive

Recovery under treatment can be expected in early cases

Pachymeningitis Cervicalis Hypertrophica

This is a subdivision of spinal meningomyelitis. The patient complains of severe pains in the neck, back and arms with weakness of the arm muscles The muscles of the arm are wasted and reflexes diminished There may be spasticity and exaggeration of the reflexes in the legs Evidence of cerebral involvement with pupillary changes, ocular palsies or aphasia may co-exist

Transverse Myelitis

Acute transverse myelitis is of sudden onset There is paralysis of the lower trunk and legs the arms rarely being affected. Sensation is lost, and there is incontinence of faeces and urine The tendon reflexes are lost if the lesion is below the centre, exaggerated if above. Trophic ulceration of the sacral area is common and often marked The Wassermann reaction is usually positive in blood and cerebrospinal fluid

The disease runs a rapidly fatal course in most cases, death ensuing from secondary infections

Erb s Syphilitic Spinal Paralysis

This is a rare condition developing some years after infection and characterized by a gradual onset of spastic paresis of the legs There is usually no sensory change, and the bladder function is little affected The reflexes are increased. Apart from the spastic gait there is no disturbance of physical or mental condition and the disease may persist without incident for many years.

Syphilitic Chronic Anterior Polio-myelitis

Symptoms of anterior horn involvement are very rare, and

may occur alone or with tabes dorsalis

There is severe pain in the affected extremities, with weakness of the muscles and later atrophy Sensation is unchanged The end result is complete paralysis and atrophy of the muscles innervated from the affected areas

A variety of other rare phenomena can be produced by spinal meningitis, myelitis and local gummatous processes. These include an acute ascending spinal paralysis, amyotrophic lateral sclerosis, syringomyelic and Brown-Séquard effects

Tabes Dorsalis (Locomotor Ataxia)

The essential pathological lesion in tabes dorsalis is a fibroblastic infiltration of the sheaths of posterior nerve roots spreading into the nerve The process is most commonly found in the lumbo-sacral region but can affect any level

The ascending nerve fibres of the cord which originate in the posterior root ganglia become degenerate. This affects the posterior columns, and from the degeneration and subsequent gliosis is derived the name tabes dorsalis. The spino-thalamic tracts carrying sensation of pain touch and temperature do not degenerate because there is a cell relay within the cord but these sensations are affected by interference with the nerve fibres in the posterior roots.

There is usually evidence of associated meningitic or myelitic lesions and cranial nerves may also be affected Argyll Robertson pupils are probably caused by degeneration of fibres connecting the visual centres in the superior corpora quadrigemina with the nucleus of the third cranial nerve.

Symptoms and signs vary considerably from case to case as does the rate of progress of the disease If a combination of effects is suggestive the diagnosis can be clarified in most cases by blood test and lumbar puncture The blood Wassermann reaction is positive in about 70 per cent of early cases. In the cerebrospinal fluid the Wassermann reaction is positive in 70–90 per cent of early cases. There is an increase in globulin and in the cell count, and the Lange test gives a luetic or high middle zone reading Very rarely blood and spinal fluid tests are entirely negative in tabes dorsalis

Symptoms The course of the disease can sometimes be roughly divided into pre-ataxic ataxic and paralytic stages.

The pre ataxic stage is one of lightning pains in the legs and sometimes in the arms, of numbness and prickling sensations in the legs, and of diminution of sexual power and desire in men.

In the ataxic stage visceral crises are common Gastric crises are sudden attacks of abdominal pain, of nausea and vomiting or both. An attack may last for a few hours or for days at a time and cease suddenly The pain and nausea are extremely severe and can reduce the sufferer to hopeless agony Intestinal crises produce lower abdominal pain and diarrhoea rectal crises are characterized by tenesmus. Renal crises simulate the pain of renal colic In vesical crises there is suprapubic pain and frequency of urination, in urethral crises there is pain along the urethra. Nasal crises with sneezing bronchial and laryngeal crises with coughing and dyspnoea and cardiac crises with precordial pain are also described

Differential diagnosis in the case of crises, particularly gastric, may be difficult, but careful examination should always discover some physical signs of tabes dorsalis sufficient to restrain the surgeon

That careful examination is rare in emergency surgery is shown by the figures quoted by Stokes of ninety-seven useless surgical operations performed on a group of one thousand tabetics. The diagnoses of gastric ulcer gall bladder disease appendicitis and salpingitis predominate.

Sexual desire fades into impotence and bladder symptoms of frequency dribbling and difficulty in starting appear

Ataxia shows itself in that the sufferer finds he cannot walk in the dark or with his eyes closed Failure of vision or diplopia may occur and trophic ulcers and arthropathies are seen at this stage.

In the paralytic stage the patient becomes wasted and bedridden The paralysis is generally due to complete ataxia rather than to a motor lesion

The progress of tabes dorsalis is usually slow and may become arrested, but rarely it may be rapid and result in death in a few months Tabetics quite often reach old age. Death in the later stages is due to intercurrent infections

Signs The ankle jerks are lost early before the knee jerks Sensory disturbance such as patches of anaesthesia to pin-prick, light touch or temperature may be found over the tibiae



Fig 74—Perforating Ulcers in a Case of Tabes Dorsalis
Results of rest and treatment are shown on right

perineum inner sides of the arms or tip of the nose Bone vibration sense is often lost in the legs Diminished sense of motion and position is a prominent feature Romberg's sign may be positive or the sufferer may be unable to touch the tip of his nose when his eyes are closed if there is cervical involvement

Sensation of pain is diminished so that the tendo Achillis or sometimes the ulnar nerve at the elbow can be squeezed without protest Laxity of muscles and ligaments may allow excessive play in joints

Argyll Robertson pupils, reacting to accommodation but not to light are found in about 80 per cent of cases Small irregular pupils differing in size are also common Strabismus and diplopia sometimes occur from involvement of the cranial nerves supplying the external ocular muscles and ptosis may be seen Optic atrophy with visual failure and pallor of the discs occurs in about 6 to 9 per cent of cases

The gait is sometimes characteristic the patient throwing

his legs high and stamping his feet down heel first Trophic or perforating ulcer of the foot is a painless lesion usually communicating by a sinus with a joint, and often misdiagnosed at first as a corn or callus (Fig 74)

Charcot's joint, or tabetic arthropathy is described under osseous syphilis. Trophic phenomena occur in 12 to 19 per cent of tabetics

Some improvement with treatment occurs in most cases and arrest can usually be obtained Re-education by Fraenkel's exercises can help the ataxic patient very markedly

The Peripheral Nerves

Apart from the cranial nerves, affection of the peripheral nervous system is rare. Secondary involvement of nerves due to pressure by syphilitic processes may occur as in osteitis or periostitis of the vertebrae gummata of muscles, etc.

Syphilitic root neuritis perineuritis, neuralgia, neuritis and polyneuritis are all described.

SYNOPSIS OF CHIEF SIGNS IN CONGENITAL SYPHILIS

EARLY

1 Skin eruptions.

2 Snuffles — sometimes resulting in saddle nose

3 Rhagades Fissuring of lips and chin

4. Enlarged spleen and liver

5 Osteochondritis and other osseous lesions. Pseudo-paralysis

LATE

1 Interstitial keratitis.

2 Hutchinson s teeth Moon s molars.

3 Eighth nerve deafness.

4 Osseous lesions sabre tibia enlargement of inner third of clavicle saddle nose perforation of palate

5 Scars about the mouth

6 Dactylitis

7 Gummata of skin and mucous membranes

8 Clutton s joints

9. Backwardness slow mental development etc

10 Visceral lesions

11 Neurosyphilis

Chapter XVII

CONGENITAL SYPHILIS

The adjective congenital as applied to the prenatal infection of the foetus with syphilis is retained as a matter of common usage. The most accurate description is prenatal syphilis

It occasionally happens that an infant is infected with syphilis in its passage through the birth canal. In such cases a primary sore appears on the head usually and the disease follows the course of an ordinary acquired infection. These rare cases are not to be included under the heading of congenital syphilis which comprises only those instances in which the foetus has been infected *in utero*

Prenatal infection with syphilis has been recognized since the early days of the sixteenth century but the final collation of clinical knowledge of the subject was not made until the nineteenth century when Sir Jonathan Hutchinson gave a classical description. Two notable phenomena were early recognized and summed up in the Laws of Colles and Profeta, but their explanation was not forthcoming until the dawn of pathological diagnosis at the beginning of this century Colles's Law stated that a healthy mother bearing a syphilitic child might nurse the said child without being infected, though it might infect others Profeta's Law stated that a healthy child born of a syphilitic mother could be nursed by the mother without being infected.

These apparent evidences of immunity have now with accurate diagnostic methods, been shown to describe, in reality cases of latency The healthy mother who bears a syphilitic child can be assumed to have syphilis and should be treated. Such a mother may have a negative blood test and have been apparently cured before this evidence of relapse. The theoretical possibility of paternal infection of the ovum, the mother escaping can, for all practical purposes, be ignored

Infection of the foetus takes place via the placenta, the organisms passing through blood or lymphatic channels. Theoretically the chances of infection are greatest in early

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9 Backwardness slow mental development etc

10 Visceral lesions

11 Neurosyphilis

organs of the syphilitic foetus and a diffuse fibrosis is evident in the lungs, liver heart, pancreas and suprarenals. The placenta may be normal, or it may be larger and paler than usual, with thickened villi and with many infarcts

Congenital syphilis can for convenience be divided into early and late stages, the former extending from birth to the end of the second year

EARLY CONGENITAL SYPHILIS

The syphilitic infant may appear quite normal at birth. Oftener the child is puny the skin is putty-coloured the hair may be scanty and wig like, and there is a general appearance of senility Very often the child fails to gain weight and is restless and irritable.

Skin and Mucous Membranes

Skin eruptions may be present at birth but usually their appearance is delayed until three to eight weeks later Rashes can make their first appearance at any age up to eighteen months.

A common and early sign is a purulent nasal discharge due to involvement of the mucosa and known as snuffles The consequent blocking of the nose interferes primarily with breathing and secondarily with feeding Saddle nose may be the result of destruction of the bone.

Cutaneous eruptions can be generalized or local in distribution. The palms and soles and the mouth and anal regions are sites of election The face and scalp are often affected Macular roseolar rashes occur but the papular type is commonest (Fig 75) A bullous syphilide is relatively common and usually present at or soon after birth. In this type the bullae are generally confined to the palms and soles, but may sometimes involve the body Oftener the body is free or shows a maculo-papular eruption Bullae are often about one-eighth to one-quarter inch in diameter but may be much larger contain serous or sero-purulent fluid, and have a dull red areola They rupture easily leaving a granulating base which may become scabbed or scaly The prognosis in the presence of bullous eruptions is poor even with treatment, and the child generally dies in a few weeks

commonest lesion is a diffuse interstitial inflammation and fibrosis, the pneumonia alba of Virchow This results in a failure of the lungs to expand and produces still birth Gummatous lesions, local and diffuse, are also encountered

Osseous System

Osteitis, periostitis and osteomyelitis may all occur in early congenital syphilis Local bone gummata also occur in rare cases Dactylitis is not uncommon Destructive gummatous lesions of the nasal septum can result in saddle nose.

A lesion peculiar to congenital syphilis is osteochondritis. This produces a widening and irregularity of the epiphyseal line which can be detected on radiological examination The process begins in intra uterine life and is detectable clinically or radiologically *in a high percentage of new born syphilitic* infants It has been stated that 90 per cent of apparently healthy infants born of syphilitic mothers show radiological evidence of osteochondritis in the long bones

The disease is encountered during the first six months of life. The long bones are particularly affected Minor degrees are often unrecognized, but in severe cases or if slipping of the epiphysis occurs paralysis of a limb may be the first warning The paralysis is fictitious produced by the pain and is sometimes called Parrot's pseudo-paralysis Examination may show enlargement and tenderness at one or several places at the ends of the long bones.

Central Nervous System

In the early stages nervous signs are usually due to a meningitis. The onset is with convulsions Kernig's sign is positive, there is neck rigidity and the anterior fontanelle bulges. Prognosis is good with adequate treatment Cerebral vascular lesions, spastic diplegia and quadriplegia are also described as rare incidents Hydrocephalus and epilepsy may occur

Miscellaneous Symptoms

Nephritis, icterus neonatorum peritonitis with ascites, and orchitis may very rarely be produced by congenital syphilis.



ACUTE IRITIS AND INTERSTITIAL KERATITIS



PAPULAR LESIONS IN EARLY CONGENITAL SYPHILIS

LATE CONGENITAL SYPHILIS

After the end of the second year the character of congenital syphilis begins gradually to alter towards the appearances associated with tertiary acquired syphilis There is no abrupt change, and localized recurrent papular and condylomatous lesions of the early type are seen even in the third and fourth years Nodular gummata can occur at the same period and secondo-tertiary lesions are quite frequent Gummata of the organs are also possible during the transition to the late stage

The signs of the late stage can be divided into two types those due to a general systemic effect of syphilis, the syphilitic stigmata, and those due to a local spirochaetal or allergic action. A child may show early signs of congenital syphilis and live to develop stigmata and other late signs. On the other hand stigmata may be found casually in an apparently healthy child. The local late phenomena can appear without the stigmata and without early signs or serological evidence of the disease may come fortuitously to light, as evidenced by the following case

A strong healthy young man of twenty-two, six feet two inches in height had an attack of ulceration of the gums and tonsils lasting for several months. His Wassermann reaction was found to be positive and he was referred as a case of secondary syphilis. Investigation showed that the oral condition was a Vincent's angina. His family history was traced, and it was found that his father had syphilis five years before the birth of the patient. The mother had never had evidence of syphilis, but had positive Wassermann and Kahn reactions in the blood as evidence of infection. The patient sister two years younger was perfectly healthy and had no pathological evidence of syphilis.

The Vincent's angina cleared rapidly with appropriate treatment and a full course of treatment for the coincidental congenital syphilis was begun

The first appearance of local evidence of congenital syphilis can be delayed as long as forty years, but is very rare after the age of thirty

Developmental Stigmata

The general effect of a syphilitic infection may be manifested in such phenomena as delayed development as shown

by late walking, late dentition and late sexual development in both sexes Impotence in the male may be due to congenital syphilis. Mental retardation may be due to syphilis, but quite frequently the congenital syphilitic child is advanced for its years even in the presence of physical evidence of the disease. Cranial bosses, scaphoid scapula and a high narrow palatal arch are also seen in congenital syphilis None of these signs can be taken alone as pathognomonic of congenital syphilis, and must always be considered in conjunction with other evidence.

More certain and sometimes positive evidence of congenital syphilis is found in the teeth. The milk teeth are not involved the stigmata are seen in the permanent dentition only Significant dental defects are said to occur in about one-third of congenital syphilitics. Delayed dentition absence of groups of teeth such as the upper lateral incisors irregularly placed and widely spaced teeth can all be found but are not alone diagnostic. The dental changes which are quite characteristic of congenital syphilis are found in the upper central incisors *Hutchinson's teeth and in the first molars, mulberry or* Moon's molars (Fig 77) Hutchinson's teeth are peg-shaped and notched on the lower border The dimensions of the base are nearly the same antero-posteriorly and from side to side and the tooth tapers downwards. The upper central incisors are often widely separated and are sometimes irregularly set. Rarely the lateral upper incisors can also be affected A Moon's molar has four imperfectly formed small cusps rising in the centre of a dome or collar of enamel The cusps are soft and soon become decayed when the characteristic appearance is lost. These last two dental deformities are certain evidence of congenital syphilis. Hutchinson's teeth have even been demonstrated radiologically before they have erupted

Skin and Mucous Membranes

Nodular nodulo-ulcerative and solitary gummata of the same appearance as those of late acquired syphilis are quite common (Fig 78) They usually occur in the first and second decades, but can appear at any time

Gummata of the tongue, fauces and soft palate also occur and can be very destructive. Ulceration of the buccal and nasal mucosa also follows periosteal gummata of the hard



Fig 77.—Late Congenital Syphilis
Left, Clutton's (knee) joints; *Right*, Hutchinson's teeth and corneal scarring after interstitial keratitis. Both pictures from the same case

palate, and the nasal mucous membrane can be affected apart from the bones and septum.

Gastro Intestinal Tract

Involvement of the stomach and intestines is very rare. Clinical evidence of hepatic changes is also unusual in spite of the invariable massive infection which is seen pathologically in the syphilitic infant. Diffuse cirrhosis and circumscribed gummata occur The subject is also considered on page 185

Cardiovascular System

Here again in spite of the early evidence of widespread involvement, clinical evidence of disease is rare. Myocardial disease and aortitis are rare and peripheral vascular disease is still rarer

The Eye

Ocular palsies due to cranial nerve involvement occur with meningeal involvement. Choroiditis, choroido-retinitis



Fig 78.—Late Congenital Syphilis Solitary gumma and saddle nose

and primary optic atrophy are also seen in cases of neurosyphilis. These manifestations are the same as those seen in acquired syphilis Iritis can occur at any stage but is rare as a solitary phenomenon

The commonest and most characteristic eye lesion is interstitial keratitis This is also the commonest lesion of late congenital syphilis, and is almost unknown in the acquired disease. 30-50 per cent of congenital syphilitics present this sign which generally appears around the age of puberty but may be earlier or much later

Changes in diet or environment seem to play a part in the onset of interstitial keratitis for the incidence of the disease in young men in the early twenties was much higher in war time than it is in peace The condition is unilateral at first but the other eye usually follows in a few weeks or months if treatment is not promptly begun The first symptoms are of photophobia and pain in the eye There is circumcorneal injection and the cornea becomes dull and hazy causing failure in vision There is usually an associated iritis Later small blood vessels invade the cornea which becomes salmon pink in colour and vision is further reduced Photophobia is intense and the eye may be very painful Resolution is slow and opacities generally remain in the cornea causing reduction in vision of varying degrees depending on the situation In less than 10 per cent of cases does complete resolution take place. Treatment must be vigorous to be of any value and the prognosis is not very good in any case Relapse is very common and treatment must be prolonged to guard against this.

The Ear

Gummatous affection of the bony structures of the ear can cause deafness, or otitis media may follow nasopharyngeal involvement, particularly in infancy Eighth nerve deafness occurs at about the age of puberty in most cases and is often associated with interstitial keratitis

Deafness may come on suddenly or gradually Sometimes onset is heralded by tinnitus and vertigo The condition is usually bilateral, and if it occurs early can be a cause of deaf mutism.

The combination of deafness, interstitial keratitis and notched teeth is known as Hutchinson s triad

Bones and Joints

Periostitis, osteitis and osteomyelitis can occur and bone lesions are much commoner than in acquired syphilis. They occur between the ages of five and twenty

Osteitis and periostitis of the long bones with laying-down of new bone is common The tibia is often involved and the bone becomes thickened antero-posteriorly The process is often most marked in the middle third of the bone, so that a sabre effect is produced (Figs. 79 80) This bowing has to be distinguished from anterior bowing in rickets. In the latter condition there is no thickening of the bone Thickening of the inner third of the clavicle is also common

Diffuse periostitis also affects the radius and ulna the tibia and fibula and the bones of the skull.

Localized gummata are less common but may occur on the skull bones or on the long bones. Destruction and necrosis is unusual apart from the nose and palate (Fig 81) where osteitis can cause perforation of the nasal septum and hard palate and collapse of the bridge of the nose (Fig 82)

Bilateral painless effusion into the knee joints, Clutton s joints, is a very distinctive sign of congenital syphilis. It usually occurs about the age of puberty Tuberculosis has to be distinguished, but here the condition is commonly unilateral and painful The elbow joints may similarly be involved

Central Nervous System

Mental retardation and occasionally precocity can occur



Fig 79 LATE CONGENITAL SYPHILIS
Sabre tibiae

with congenital syphilis. Nervous irritability is said by Stokes to be very common

Most of the types of acquired neurosyphilis are reproduced by congenital syphilis, and asymptomatic nervous involvement as shown by an abnormal cerebrospinal fluid is quite common

Meningeal and meningovascular phenomena can occur at any age. Juvenile tabes dorsalis is milder than the acquired form and may only be found on routine examination Ataxia and visceral crises and lightning pains are seldom pronounced

but bladder symptoms and optic atrophy are common The age of onset is about fifteen

Juvenile general paralysis of the insane usually appears about the age of puberty but may be delayed until later The delusions of the adult are not seen, the child becoming mentally degenerate, forgetful and unteachable. The habits are dirty and incontinence is common Convulsions may occur Paresis sine paresi is also found in congenital syphilis

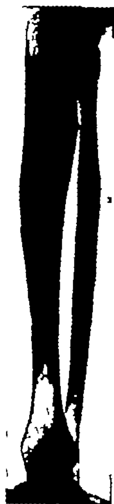


Fig. 80.—Late Congenital Syphilis Periostitis of tibia

Third Generation Syphilis

A congenital syphilitic woman cannot infect her husband, but there is evidence that, very rarely she may infect her children. It is the present view that such women should receive antisyphilitic treatment during pregnancy whether there is evidence of activity of the disease or not.

The male congenital syphilitic is sometimes impotent, but he can safely be allowed to marry for there is no risk of his infecting his wife

A congenital syphilitic may become the victim of acquired syphilis.

Diagnosis of Congenital Syphilis

In the absence of physical signs of disease, treatment of the infants of syphilitic mothers should be delayed and the children watched and their blood tested frequently A healthy child of a mother with a positive blood test may be born with a positive reaction but revert to negative after a few weeks. On the other hand the child of a treated mother may be born with a negative blood reaction and later revert to positive.

In a recent case a treated mother produced a healthy child with a negative blood Wassermann reaction Two weeks later the child developed snuffles and the blood test became positive.



Fig 8 —Late Congenital Syphilis
Saddle-nose and ulceration of palate



Fig 8 —Late Congenital Syphilis
Left, complete destruction of soft palate *Right*, same [illegible] result of plastic repair of saddle nose

Expectancy is therefore advised but if for any reason treatment is begun on an apparently healthy child it must be continued to the bitter end or more harm than good will be done if the child is indeed syphilitic

If the diagnosis of congenital syphilis is made at any time it is the physician s duty wherever possible to try to examine, or have examined all members of the patient s family and to put under treatment any who show signs of disease.

Chapter XVIII

TREATMENT OF SYPHILIS: GENERAL

INTRODUCTION

The treatment of a case of syphilis is not merely a matter of routine injections once a diagnosis is made. Syphilis is liable to infinite variations both before and during treatment, and every case is entitled to individual evaluation not only at the *time of diagnosis but every time it is seen.* Age, sex, general condition have all to be considered and treatment may have to be altered in quality or in quantity according to response or because of toxic reactions A fundamental principle is to use the most potent available drugs appropriate to a given case and to insist that treatment continues regularly and without interruption. Progress must be controlled by adequate pathological tests.

Patients must be clearly told about the nature of the disease and given an outline of the major complications of treatment They should know the length of time treatment is likely to last and understand the grave dangers of inadequate or haphazard treatment

A preliminary general overhaul must be routine in every case whether internal involvement is suspected or not and before each treatment the patient should be examined stripped if possible, for evidence of any toxic phenomena such as jaundice and skin eruptions The urine should be tested on each visit for albumin bile, and if possible for urobilinogen with Ehrlich's reagent A check should be kept on the weight.

Every patient as soon as possible after treatment has rendered him non-infectious should be sent to his dentist to have his teeth and gums put into the best possible condition *A healthy mouth at the start is far less liable to be affected by* the heavy metals and the patient can thus avoid not only discomfort but also possibly delay in treatment

Adequate rest and avoidance of over work is of paramount importance in syphilis as in any other disease Mental stress must be avoided and the physician can do a great deal in this direction by his preliminary explanation to the patient

In marital cases where the partner has been unwittingly exposed to infection it will be wise to advise frank explanation and to discuss the prospects with both parties.

Complete rest in early cases until the lesions have healed is of the greatest value as shown by the results obtained in men in the Services who react better to treatment than their counterparts in civil life who must continue working

Alcohol should be prohibited and smoking is contraindicated in the presence of mouth lesions at any stage.

Sexual intercourse should be avoided in early cases during the whole course of treatment and for a year after In certain instances the resumption of coitus may be permitted as when a married couple are both infected, but pregnancy must not occur In such cases a full six months of preliminary treatment is necessary and a condom must always be used.

LOCAL AND NON-SPECIFIC TREATMENT

The Chancre

It cannot be too often emphasized that until a positive diagnosis is made, only saline solution should be used as a dressing for genital sores. Antiseptics kill surface spirochaetes and reduce enormously the chances of finding the organism by dark-ground examination. If chancroid is suspected, sulphonamide treatment is not contra-indicated for it does not affect *S pallida*.

Once diagnosed, the nature of the local application is not of great importance, for the main therapeutic effect will come from the specifics. Simple cleanliness and the use of an ointment such as 33½ per cent calomel or ammoniated mercury or of a dusting powder is usually sufficient.

A coincident phimosis may require a dorsal slit or circumcision or an inguinal bubo may have to be incised. Apart from secondary infection and suppuration, the adenitis of syphilis needs no treatment.

Cutaneous Secondary Lesions

Crusted secondary lesions should be treated with antiseptic baths, removal of scabs and application of ammoniated mercury ointment.

Moist condylomata should be covered with a dusting

powder Ultra violet light twice weekly is sometimes useful in hastening the disappearance of syphilides, particularly the pigmented variety This form of treatment has also been used in cases of secondary syphilis relapsing in spite of adequate treatment.

For ulceration in the mouth potassium chlorate or phenol gargles can be used

Ulcerative Gummata

The large ulcerative gumma should be treated locally by cleansing with hydrogen peroxide and the application of eusol or Lotio Rubra. Occlusion with Elastoplast is sometimes effective.

Late Syphilis

In cardiovascular and nervous syphilis it is important to see that the patient adapts his activities to fit his physical and mental capacity An ordered regular life is essential

Fever therapy is a non-specific measure of the greatest importance in late neurosyphilis and may yet have its application in the earlier stages of the disease. This is discussed fully on page 347

Surgical and orthopaedic measures are important in osseous syphilis, and in the treatment of trophic phenomena due to nervous syphilis.

Ultra violet light therapy autohaemotherapy and protein shock therapy all have a place in certain cases as for example in Wassermann fastness.

THE SPECIFIC TREATMENT OF SYPHILIS

Certain drugs exert a general curative effect in syphilitic infections which entitles them to be classified as specifics. These are the arsenicals bismuth and mercury and they are shown in order of potency

The iodides are considered with the specifics, for though they have no lethal effect on spirochaetes they have an important place in the treatment of late syphilis

Mercury has been used in the treatment of syphilis as long as the disease has been known and still retains its place as an important weapon at certain stages Mercurials were used

for skin diseases in the pre-Columbian era and their use in syphilis, when it appeared, is not surprising The iodides have been in use for a little more than a hundred years.

After four centuries of syphilis, the first major advance in treatment came in 1909 with the discovery by Ehrlich of arsphenamine. This was the first safe arsenical for use in human syphilis, and it is still the most potent drug available. Previously a pentavalent arsenical atoxyl had been tried but it had a grave drawback in that it caused optic atrophy Ehrlich's experiments began from the basis of atoxyl and his 606th compound was arsphenamine

Arsphenamine did not fulfil the original hope that one injection would cure syphilis, but its effects on the clinical phenomena were spectacular after mercury Increasing the number of injections of arsphenamine was tried after relapses had occurred from one injection but even this was not altogether successful and it was eventually obvious that mercurial treatment had to be combined

This combination was used until the establishment, in 1922 of bismuth as a more potent antisyphilitic agent than mercury It is now known that the best results in early syphilis are obtained by the combined use of the specifics, though normally this can be taken to mean an arsenical and bismuth.

Since arsphenamine a great variety of arsenicals has been elaborated, neo-arsphenamine (Ehrlich's 914) and arsenoxide being probably the most important. Arsenoxide (for example, Mapharside or Neohalarsine) can be considered a rediscovery as a similar compound had been prepared by Ehrlich.

Penicillin has been shown to be an effective spirochaeticidal agent. Its applications and modes of use in the various stages of syphilis are considered in Chapter XX.

THERAPEUTIC SHOCK AND THERAPEUTIC TESTS

The phenomenon of an increase in degree of early cutaneous manifestations after injections of mercury was first described by Jarisch in 1895 Herxheimer added to the interpretation, and therapeutic shock is now often referred to as Jarisch-Herxheimer reaction.

When arsphenamine came into use, therapeutic shock

became more frequent and it was obvious that all the tissues shared in the reaction The reaction is one of inflammation and oedema at any focus of spirochaetal infection and the effect is usually noticed after the first or after one of the first few injections.

Shock is rare and unimportant after mercury and bismuth but is fairly common after the arsphenamine series of drugs. The cutaneous therapeutic reaction of the early stages is of no consequence but visceral reactions are to be feared in the late stage, and arsenic should always be used with caution in latent or visceral syphilis, often only after preliminary treatment *with mercury or bismuth. To start a patient with* aortitis on treatment with arsenic at once might produce a fatality from a resulting local inflammation and oedema which could block up the openings of the coronary arteries. Involvement of the liver and nervous system are other important types in which a gentle building up of treatment is indicated

Provocation of a positive blood test by the injection of neo-arsphenamine in a sero-negative case can be included under the heading of therapeutic shock

The use of the specifics is sometimes indicated as an aid to diagnosis when pathological tests fail partially or entirely to substantiate a clinical diagnosis. Therapeutic tests are never indicated in early syphilis and occupy only a minor and precarious position in the field of diagnosis Some indications are chronic superficial glossitis chronic leg ulcers and tumours of the nervous system liver lungs or bones. In these last cases *the test should not be so prolonged as to jeopardize the patient's* chances of a successful result from operation if cancer is also suspected

A therapeutic test can only be considered positive when improvement is definite and progressive It should be remembered that arsenic and bismuth have a non-specific effect in certain skin diseases for example lichen planus and in other conditions such as lung abscess, Vincent's angina and some forms of tuberculosis

That the discussion of therapeutic tests has not been included under the general heading of diagnosis is intended to point out its relative unimportance and to ensure that they should have no place in the investigation of early syphilis

MERCURY

The action of mercury is not fully understood The concentration of mercury necessary for a lethal effect *in vitro* cannot be supported *in vivo* Mercury probably has a spirochaetostatic action rendering the organisms more liable to attack by defence mechanisms of the body and may possibly have a stimulant effect on tissue defences or a direct action on the metabolic enzymes of *S pallida*.

Mercury now has only a limited use in late syphilis, and will seldom be used in the early stages except as an adjuvant. It is contra indicated when a more potent drug can be used and in the presence of nephritis.

The mouth must be in best condition before treatment begins. Administration is effected in a number of ways, and the general intention should be to introduce as much of the drug as possible without producing toxic effects

Oral Administration

Mercury can be given in the form of Pilula Hydrargyri cum Ipecacuanha (Hutchinson's pill) in doses of one pill thrice daily Each pill contains one grain each of mercury with chalk and compound ipecacuanha powder The green iodide of mercury can also be given in pill form in half-grain doses thrice daily

An excellent combination of mercury and iodide for use in late syphilis is Mistura Hydrargyri Iodidi

Solution of mercuric chloride	1 drachm
Potassium iodide	10 to 60 grains
Fowler's solution	5 minims
Compound infusion of gentian to	½ ounce

Dose ½ ounce thrice daily after meals.

Intravenous Injection

Mercury by this route is very quickly excreted and if it is to be effective the injections must be given very frequently daily or every other day The cyanide, perchloride and biniodide have been used in doses of 1–2 c.c. of a 1 per cent solution, and various proprietary solutions of other salts can be obtained.

The method will seldom be chosen but if it is, a convenient preparation is Collosol mercury sulphide in doses of 2 5 c.c

Intramuscular Injection

Mercury perchloride or biniodide are soluble preparations which can be given intramuscularly in doses of 1 c.c of a 1 per cent solution equivalent to ⅙ grain To be effective the injections have to be daily or every other day over periods of 6–8 weeks so that this method has little application Insoluble preparations such as Lambkin's cream or Squire's cream (mercury suspended in fatty bases) calomel cream and mercury salicylate suspensions in various bases are more slowly absorbed and can be given once or twice weekly

Collosol mercury sulphide is probably the most effective drug for intramuscular use, and is relatively painless. The dosage is 2 c.c. once or twice weekly The injections are made into the gluteal muscles as described on page 339

A close watch must be kept on the urine and on the state of the mouth

Inunction

Mercury applied to the skin by inunction is absorbed from that part of the ointment which penetrates the mouths of sweat glands and hair follicles Inunction is a safe controllable and effective way of introducing the drug when the treatment is properly done Its application is restricted to hospital practice and to the intelligent patient

Ung Hydrargyri (B P) mercury suspended in benzoated lard is used in quantities of 4 gm. per treatment The ointment is rubbed in six nights a week in courses of six to eight weeks with rest periods of one month between courses.

The hairless skin is used to avoid follicular infections, and the area chosen is first washed with soap and water and dried with spirit At least half an hour is spent on gently but firmly rubbing the ointment into an area eighteen inches in diameter

The first rub is done on the left hand side of the chest the second on the right The third rub is done on the left side of the abdomen and flank, the fourth on the right The fifth and sixth rubs are done on the inner sides of the left and right thighs.

After a rub the excess ointment should be wiped off with

dry gauze. On the seventh day a bath takes the place of the rub and the body is washed and dusting powder applied.

Indications for the Use of Mercury

The only real indication for mercury at the outset is late cardiac or hepatic syphilis, and then only as an introductory measure. Patients intolerant to arsenic may be treated with bismuth and mercury and on long sea voyages when no doctor is available, mercury may have to be used Intramuscular injection or inunction will usually be preferred as the most potent.

Mercury has no longer any place in the treatment of early syphilis

Complications

Stomatitis Unless a patient starts off with a healthy mouth complications are very likely Salivation is a forerunner of stomatitis and gingivitis in which the buccal mucosa becomes red, oedematous and sore and may even ulcerate. Pus collects in the gum pouches and in former days it was not uncommon for treatment to continue until the teeth were loosened in their sockets A dark line may form at the gum margin.

Prophylaxis consists in oral hygiene, brushing the teeth after meals and massaging the gums In an established stomatitis the mouth should be washed out with sodium bicarbonate solution and hydrogen peroxide. Treatment must be reduced or stopped temporarily

Skin Eruptions Follicular infections occur sometimes with inunction particularly on the hairy skin Another form of medication must be used, and the local condition treated with calamine lotion.

Rarely generalized eruptions of a scarlatiniform or morbilliform character can arise after any type of mercurial treatment, and coincident herpes zoster has been reported. Treatment will consist of withdrawal of the drug and the application of a soothing cream or lotion

Gastro-intestinal Disturbance Particularly after oral mercury diarrhoea is not uncommon and may be accompanied by tenesmus. Actual colitis and ulceration have been reported

Discontinuing the drug, combined with sedatives such as Dover's powder soon cures the condition, and treatment can

be resumed with reduced doses.

Renal Complications Mercury is never to be used when there is existing kidney damage Nephritis or nephrosis can result from mercurial treatment. Albumen in the urine is the first sign and indicates immediate cessation of treatment This is a most important and serious complication and must be guarded against by routine testing of urine each week.

THE IODIDES

The nature of the indirect action of the iodides on the lesions of late syphilis is still obscure. Other granulomata such *as those of leprosy blastomycosis or actinomycosis* are also benefited by iodides. There is no action whatsoever on *S pallida*. Because of their general action in granulomatous conditions iodides must not be used in therapeutic tests.

Iodides may aid the penetration of the specific drugs* The indications for their use arise in late syphilis and they are of value in gummatous conditions of skin mucous membranes, bones or liver and in cardiovascular syphilis. They are useful also in neurosyphilis of the meningitic or meningo vascular types and may possibly be of some use in latency The iodides are to be considered only as adjuvants.

Administration

Sodium or potassium iodide can be administered orally in doses of 10–60 grains three times daily The dose should be taken before meals well diluted with water or milk.

Mist Hydrarg Iodidi (see p 239) is a useful preparation for treatment in late syphilis

There is evidence that intravenous sodium iodide is valuable *in non parenchymatous neurosyphilis even without specific* therapy

After oral administration to test for intolerance a daily injection *of sterile 10 per cent sodium iodide solution is given* intravenously each day *The first dose is 25 c.c* increased by this amount daily until top dosage of 100 c c is reached A course lasts six days a week, for five weeks

Bismuth treatment is also given and the whole is a preliminary to the use of arsenicals *Iodides are contra indicated* in pulmonary tuberculosis and with thyroid adenoma

Complications

Acute poisoning is very rare even with intravenous therapy Angio-neurotic phenomena including oedema of the glottis can occur and multiple cutaneous haemorrhages are also described. Milder phenomena are common, but signs of intolerance often disappear if the dosage is doubled. Mild iodism simulates a cold in the head with running nose, sore eyes, coughing and sneezing Enlargement of the salivary glands can occur Bad taste in the mouth, anorexia nausea, vomiting and diarrhoea are signs of gastro-intestinal intolerance

Acneiform eruptions on the chest, back and face are usually not sufficient to cause withdrawal of the drug Other eruptions of a scarlatiniform, morbilliform, eczematous or bullous type are rarely seen. Acute bullous iodide dermatitis may be very severe and even fatal. The drug may have to be withdrawn in cases of severe dermatitis

BISMUTH

Although bismuth had been tried in human syphilis as early as 1889, its full value and application was not realized until 1922 after the work of Levaditi and others.

Mercury was quickly displaced as the heavy metal adjuvant to arsenic in syphilis, because bismuth is much more effective, occupying an intermediate position between mercury and the arsenicals It is also less toxic than mercury

Bismuth is essentially a companion to the treatment with arsenicals, but in some cases it may be used alone from choice or from necessity

Mode of Action

The recent work of Eagle makes it appear probable that bismuth exerts its spirochaeticidal action like the arsphenamines by combining in the spirochaete with enzymes concerned with its vital processes. The action is experimentally unaffected by the absence of oxygen or tissue fluids.

In early syphilis bismuth is superior to mercury but slower and less reliable than the arsphenamines. *S pallida* disappears from surface lesions only after days and the lesions themselves heal much more slowly than with arsenical treatment. Clinical and serological relapse is common if only bismuth is used in

the early stages. Bismuth is less toxic than mercury and combined arsenical and bismuth therapy is vastly superior to arsenic and mercury

Administration

For practical purposes it can be said that bismuth can be given safely only by intramuscular injection. Intravenous injection produces toxic effects which are often fatal and is completely ruled out Oral administration of Sobisminol Mass has certain drawbacks and dangers which limit its use, and it can have no place in treatment until more experimental work has been done.

Preparations for Intramuscular Injection

Bismuth preparations are classified according to solubility and solvent A vast number of proprietary brands are available and any type preparations made by a reputable manufacturer can be accepted Only a few well known examples of each important class are given

(1) *Aqueous Suspensions of Metallic Bismuth* Bismostab (Boots) and Bisglucol (May and Baker) contain 0·2 gm bismuth in each c.c of isotonic glucose solution In the same category comes Chlorostab (Boots) which is a suspension of bismuth oxychloride in water

The unit dose of all these preparations is 1 c.c.

(2) *Suspensions in Oil* Bisantol (May and Baker) is a 10 per cent suspension of bismuth salicylate in neutral vegetable oil. Unit dose 2 c.c Bicreol (Burroughs Wellcome and Co) is an oily suspension of bismuth metal containing 0·15 gm. per c.c. Unit dose 2 c.c Rubyl May and Baker) is a suspension of quinine iodo-bismuthate Unit dose 3 5 c.c

(3) *Aqueous Solutions* Thiobismol (Parke Davis and Co) This is sodium bismuth thioglycollate and is given in a dose of 0·2 gm. dissolved in 1 c.c. of water at least twice weekly

(4) *Oily Solutions* Neocardyl (May and Baker) contain bismuth butylthiolaurate. Unit dose, 2 c.c Stabismol (Boots) contains bismuth α-carboxylcyclohexanylacetate Unit dose 2 c.c

Choice of Preparation

Many theories have been advanced about the potency and

special properties of various bismuth preparations, but none has been proved

The basis of selection is that if a rapid effect is wanted a rapidly absorbed soluble preparation such as Thiobismol should be used, and if a slower but more sustained effect is aimed at, an insoluble preparation is indicated.

Thiobismol would be used daily or every other day in early neurosyphilis, combined perhaps with iodide therapy as a preparation for an arsenical

In the routine treatment of syphilis a bismuth metal aqueous suspension gives excellent results and causes the least discomfort after injection. Some patients, however may find an oily suspension pleasanter and it matters little which preparation is used so long as dosage is on the lines indicated Bismuth should form a constant protective background with the more potent action of courses of arsenicals superimposed.

The method of intramuscular gluteal injection is described on page 339

Suspensions should be well shaken before the dose is withdrawn from the vial and some oily preparations may have to be warmed before they can be drawn up into the syringe.

Accidental intravenous injection has to be avoided and injection should be followed by vigorous massage for a few minutes. Exercise is not contra-indicated After the first few injections discomfort is very slight and fleeting

Complications

Complications from the use of bismuth are rarely sufficiently grave to cause cessation of treatment when the drug is properly administered Therapeutic shock can occur but the risk is slight at any stage. Bismuth-resistant syphilis is extremely uncommon, and in early cases completely intolerant to arsenic, good results can be obtained with prolonged bismuth therapy

Pain. Local pain at the site of injection can be avoided by good technique and sharp needles. Injection of a c.c. of air after the fluid will allow a clear track to be left on withdrawing the needle. This, with massage and hot baths will help most cases. A change of preparation can also be tried if pain is persistent.

Abscess Sterile abscess in the buttock sometimes occurs and oily preparations are almost always to blame A deep

tender swelling is felt but incision is rarely necessary Fomentations and hot baths usually suffice. If the injection is too shallow hard lumps of bismuth remain for a long time in the subcutaneous fat.

Accidental Intra-arterial Injection. This is a very rare accident resulting in extreme local pain The skin over the affected area shows a purpuric eruption and necrosis of a wedge of tissue may result in sloughing The patient is confined to bed and treatment consists of sedatives and hot applications

Accidental Intravenous Injection Oil embolism in the lungs with certain preparations may cause pain in the chest and coughing and grave shock or even death have been reported

Any preparation reaching the blood stream can produce signs of acute bismuth poisoning The signs may include haemorrhagic skin eruptions, stomatitis, nephritis and bronchopneumonia. The condition may prove fatal

Intravascular injection is completely avoided by careful technique

Bismuth Line It is rare for a patient on bismuth therapy to avoid having at least a slight bluish line of pigmentation at the gum margin. This in itself is no indication for stopping treatment The sign is least evident in those patients who have started off with a clean mouth Stomatitis usually occurs in a patient who already has some pyorrhoea In such cases pigmentation can be very pronounced and may be seen on the cheeks and even on the hard palate

Treatment is as already described for mercury stomatitis

Dermatitis Toxic skin eruptions are uncommon The lesions may simulate pityriasis rosea appearing as a widespread crop of reddish-brown plaques and papules with a little superficial scaling The eruption fades on withdrawing the drug but reappears if treatment is begun again. Exfoliative dermatitis during bismuth therapy has been described

Hepatitis Jaundice occurring during bismuth therapy has often been described but as the patients have usually had some arsenical treatment in the past it is only rarely that bismuth can be inculpated as a likely factor

The known fact of linkage of bismuth with glutathione would suggest that the drug has theoretically some hepatotoxic action It is however quite safe and absolutely essential to continue therapy with bismuth during the course of any

intercurrent hepatitis occurring with antisyphilis treatment.

Renal Complications Albuminuria sometimes arises during bismuth therapy and a true nephritis may occur Cessation of bismuth treatment is quickly followed by the disappearance of albumen from the urine and the drug can be used again after a short rest. Grave renal damage is very rare and is avoided by precautionary testing of the urine at every visit

Miscellaneous Reactions Peripheral neuritis is a rare complication, and herpes zoster may sometimes occur during bismuth therapy After recovery bismuth can be used again Gastro-intestinal upset, including diarrhoea, may be due to bismuth Some patients exhibit curious signs of intolerance after each injection with malaise, fever headache and general aching pains rather like influenza. The reactions may be bad enough to necessitate cessation of bismuth therapy

Jarisch-Herxheimer reactions are rarely severe because bismuth is not rapidly spirochaeticidal.

THE ARSENICALS TRIVALENT COMPOUNDS

Mode of Action

It is now reasonably certain that the arsenicals of the arsphenamine series are oxidized in the body to arsenoxide and in this form become spirochaeticidal The possibility of a direct action of arsphenamine and neo-arsphenamine on *S pallida* is not excluded but this method of attack is probably secondary The lethal action of the arsphenamines on *S pallida* in the body is developed only after a latent period — presumably for oxidation — but arsenoxide is immediately effective. Although arsenoxide is active *in vitro* in the absence of oxygen, arsphenamine in similar circumstances is negligibly spirochaeticidal

It is believed that arsenoxide combines with a glutathione-like substance present in *S pallida*. The resulting compound is incapable of performing the part played by glutathione in the respiratory metabolism of the parasite.

The affinity of arsenoxide for substances containing sulphur as a sulphydryl group, for example, glutathione, cysteine, etc., is demonstrable experimentally *in vitro* and *in vivo* The addition of sulphydryl-containing substances can protect *S pallida* by binding arsenoxide.

tender swelling is felt but incision is rarely necessary Fomentations and hot baths usually suffice. If the injection is too shallow hard lumps of bismuth remain for a long time in the subcutaneous fat.

Accidental Intra-arterial Injection. This is a very rare accident resulting in extreme local pain. The skin over the affected area shows a purpuric eruption and necrosis of a wedge of tissue may result in sloughing The patient is confined to bed and treatment consists of sedatives and hot applications.

Accidental Intravenous Injection Oil embolism in the lungs with certain preparations may cause pain in the chest and coughing and grave shock or even death have been reported

Any preparation reaching the blood stream can produce signs of acute bismuth poisoning The signs may include haemorrhagic skin eruptions, stomatitis, nephritis and bronchopneumonia. The condition may prove fatal

Intravascular injection is completely avoided by careful technique

Bismuth Line It is rare for a patient on bismuth therapy to avoid having at least a slight bluish line of pigmentation at the gum margin This in itself is no indication for stopping treatment The sign is least evident in those patients who have started off with a clean mouth. Stomatitis usually occurs in a patient who already has some pyorrhoea. In such cases pigmentation can be very pronounced and may be seen on the cheeks and even on the hard palate

Treatment is as already described for mercury stomatitis.

Dermatitis Toxic skin eruptions are uncommon The lesions may simulate pityriasis rosea appearing as a widespread crop of reddish brown plaques and papules with a little superficial scaling The eruption fades on withdrawing the drug but reappears if treatment is begun again Exfoliative dermatitis during bismuth therapy has been described

Hepatitis Jaundice occurring during bismuth therapy has often been described but as the patients have usually had some arsenical treatment in the past, it is only rarely that bismuth can be inculpated as a likely factor

The known fact of linkage of bismuth with glutathione would suggest that the drug has theoretically some hepatotoxic action It is however quite safe and absolutely essential to continue therapy with bismuth during the course of any

The bearing of this property of arsenoxide is important in the consideration of hepatitis occurring during the course of treatment of syphilis (see also p 188) The reason for the apparently selective action of arsenoxide on the sulphydryl compounds of the parasite more than on those in tissue is not known

The arsphenamines disappear from the blood within a few minutes of injection, and are stored mainly in the liver and spleen where conversion to arsenoxide takes place. Excretion takes place through the kidneys and bowel Maximum elimination takes place in the first forty eight hours, and is to all intents and purposes complete in seven days Certainly there is no actively spirochaeticidal arsenic left after this time Any that remains is inactive though potentially toxic.

There are theoretical and practical grounds for believing that the spirochaeticidal effect is more prolonged after an injection of an arsphenamine than after an injection of arsenoxide, and it would appear that if the latter is used injections should be given at least twice weekly

Choice of arsenical will therefore sometimes be governed by availability of the patient.

Arsphenamine (Salvarsan 606 ')

Ehrlich discovered this first effective arsenical in 1907 It is still considered to be the most active and efficient drug available for the treatment of syphilis.

Arsphenamine is supplied in ampoules as the hydrochloride, an amorphous yellow powder containing 32 per cent of trivalent arsenic. Before injection it must be neutralized with sodium hydroxide to produce, first, the insoluble arsphenamine base, and later with excess alkali the monosodium and disodium salts. This process of alkalization must be carefully and exactly performed for accidental injection of acid arsphenamine is often fatal.

The total volume is made up with water so that 0·1 gm. is contained in 20 c.c of solution and intravenous injection is made by the gravity method

The average dose of arsphenamine is 0·4 gm and the maximum dose is 0·6 gm. Injections are given once weekly in six to eight week courses, a total of 24-32 injections being

usual in early syphilis. Bismuth therapy forms an essential background

Arsphenamine is not suitable for use in general practice and has indeed entirely fallen into disuse in Britain For this reason technical details are omitted

Neo-arsphenamine (914 ')

Ehrlich followed up his discovery of Salvarsan by searching for a soluble arsphenamine which would not require alkaliza tion. The result of his 914th experiment was neo-arsphen amine a bright yellow powder soluble in water and ready for use without further preparation It contains 19 to 22 per cent of trivalent arsenic

The drug is unstable and deteriorates rapidly in solution or on exposure to air It is supplied in sealed ampoules containing from 0·15 to 0·9 gm The average adult dose ranges from 0·3 to 0·6 gm.

A number of manufacturers supply neo-arsphenamine *Among the preparations approved by the Ministry of Health are* Neosalvarsan (Bayer) Novarsenobillon, N.A.B (May and Baker) Neokharsivan (Burroughs Wellcome) and Novostab (Boots)

Preparation and Administration. Ampoules must be carefully examined for cracks and for signs of deterioration of the contents *Immersion of the ampoule in spirit shows up any* defects in the glass. If the powder is dark yellow orange or brown in colour the ampoules must be discarded

The ampoule is opened by breaking off the neck and the yellow powder is shaken out on the surface of 10 c c of sterile doubly-distilled water contained in a sterile gallipot or wide necked glass bottle. Solution takes place without agitation or shaking after about thirty seconds Squirting with a syringe to hasten solution is likely to increase toxicity

Before the resultant clear yellow fluid is drawn up into a 10 c.c. Record syringe it is permissible to swirl it gently round the gallipot once or twice to ensure equality of distribution

Injection must be intravenous and the greatest care exer cised to ensure that none of the drug escapes into the tissues The needle should be wiped before it is introduced If the patient complains of pain or burning sensation during the injection or if there is any swelling the needle must at once be withdrawn and another vein used

Immediate toxic reactions are very often due to rapid injection. The ideal rate of injection is said to be 0·1 gm per minute, but in practice if one minute is spent in administering the whole dose no complications are likely to arise. The use of a fine-bore needle will curb the hasty

Neo-arsphenamine is the arsenical most commonly used in Britain and its proper dosage, effects and potency are well known If treatment must be confined to weekly visits, this is the arsenical to be used. The ampoules should be stored in a cool dark place, when they will remain safe for use for years.

Stabilarsan (Boots)

Arsphenamine diglucoside or Stabilarsan contains 21 per cent of trivalent arsenic It is obtained in ampoules containing a solution of the drug in 50 per cent glucose, ready for intra venous injection without further preparation as soon as it is drawn into a syringe. The average adult dose is 0·3 to 0·6 gm.

Stabilarsan is less potent than neo-arsphenamine. The advantage of ease in administration is slightly counterbalanced by the fact that the time in which it is safe to use a particular batch is only a few months. The end date of safety is indicated clearly on each box and ampoule, and the practitioner using this preparation should avoid overstocking

Silver Arsphenamine

This preparation contains 19 per cent of trivalent arsenic and is a dark-brown powder which dissolves in water to form a clear solution like black coffee. It has about the same thera peutic value as neo-arsphenamine and has the reputation unconfirmed, of having a special application in neurosyphilis.

The average dose in early syphilis is 0·3 gm given once weekly in courses of eight to ten weeks for about forty injections Bismuth is given concurrently

Neo-silver arsphenamine is a combination of silver arsphenamine and neo-arsphenamine with an average adult dose of 0·4 gm. given weekly in courses as already described for silver arsphenamine.

The use of either of the silver preparations is contra indicated except when advised by a specialist venereologist.

the proper spacing of dosage has been fully investigated may be the equal of arsphenamine.

Neohalarsine (May and Baker) Neohalarsine is 3-amino-4 hydroxyphenylarsine-oxide tartrate dihydrate This is a white powder supplied in ampoules It is given intravenously dissolved in 10 c c of distilled water in doses of 0·03–0·09 gm The standard dose is 0·09 gm. The general description is as given above for Mapharside. The author has used this drug in many hundreds of cases at all stages of syphilis. The results after long term or intensive treatment are the same as with Mapharside.

THE ARSENICALS : PENTAVALENT COMPOUNDS

Atoxyl sodium arsanilate was the original arsenical tested in experimental trypanosomiasis, and was the chemical basis from which Ehrlich's work began In spite of its name Atoxyl was very toxic, particularly to the eye, and was not very effective in syphilis It is not now used and is mentioned only for interest

Tryparsamide

A derivative of Atoxyl tryparsamide is a pentavalent compound containing 25 per cent of arsenic Tryparsamide is supplied in ampoules as a white powder which is dissolved in 10 to 20 c.c of sterile distilled water and injected intravenously Solution takes place slowly and can be assisted by shaking or squirting with a syringe Injection may be made rapidly without danger

Tryparsamide is not a member of the arsphenamine series and is quite valueless except in neurosyphilis, particularly of the parenchymatous type when it can be used alone or with fever therapy

The only real danger in its use is the possibility of optic nerve damage and patients must be carefully studied before and during treatment so that therapy can be immediately stopped if signs of optic atrophy appear Examination includes the estimation of visual fields visual acuity and state of the fundi.

Dosage begins with 1 gm then 2 gm and continues at the normal of 3 gm weekly for courses of ten weeks or more

Bismuth is given concurrently A very long period of treatment is often necessary to produce results, and hope need not be abandoned if there is no great response in the first few courses.

Tryparsamide penetrates into the nervous system in every case, perhaps because of its crystalloid structure, and may there assume spirochaeticidal powers through some combination with chemical constituents of the nervous structures

Acetylarsan

Acetylarsan is the diethylamine salt of acetarsol It is supplied in ampoules as an aqueous solution each c c of which contains the equivalent of 0·05 gm arsenic in pentavalent form. A special solution for infants contains the equivalent of 0·02 gm arsenic per c.c.

Although Acetylarsan is not an arsphenamine, the clinical results of its use are comparable with those obtained with trivalent arsenicals. In potency it falls below the arsphenamines but above the bismuth preparations, and the author has found it very satisfactory for use in cases intolerant to drugs of the arsphenamine series

Administration is by intramuscular injection, which is quite painless. Excretion is very rapid, so that best results in early syphilis can only be attained if it is given twice weekly

Dosage for adults is 3 c.c twice weekly in eight to ten week courses with bismuth. If administration is confined to once weekly the dose is 5 c c.

Toxic effects are rare and, provided bi weekly treatment is possible, Acetylarsan can be used instead of sulpharsphenamine in those rare cases where intravenous therapy with an arsphenamine or arsenoxide is impossible. It should not be used for initiating treatment in early syphilis.

In the treatment of early congenital syphilis Acetylarsan is most valuable.

Acetarsol (Acetarsone Stovarsol)

Acetarsol is a pentavalent arsenical containing 27 per cent of arsenic, which can be administered by mouth. In doses sufficient to produce clinical improvement it frequently causes serious toxic reactions.

J E. Moore (*Modern Treatment of Syphilis* 1942) reviewing

the knowledge of the subject of oral arsenical treatment of syphilis is entirely against the use of acetarsol in adults and sceptical of its value in congenital syphilis. Acetarsol had a vogue as a prophylactic against syphilis, but its value in this respect was never properly assayed and is probably nil. It might be prescribed occasionally for patients who are unable to obtain injection treatment but then only after specialist consultation

GENERAL OBSERVATIONS ON THE ARSENICALS

The ideal in the treatment of syphilis is to choose the most potent drug available and applicable in a given case. In general trivalent arsenicals will be used for early syphilis and the choice will lie between neo-arsphenamine and arsen oxide. In adequate dosage either will give excellent results in combination with bismuth therapy For patients who cannot have intravenous therapy sulpharsphenamine or Acetylarsan with bismuth are available

Pentavalent arsenicals, of which tryparsamide is the most important example, are of greatest value in parenchymatous neurosyphilis but will not be chosen for early syphilitics.

The assay of efficiency of the arsenicals is difficult and can be made only on clinical results In the case of tryparsamide the concentration of the drug in the cerebrospinal fluid is never as great as is obtained with the arsphenamines, yet its value in neurosyphilis is very much greater Clinical assay of the arsphenamines can be roughly made on their ability to cause (*a*) the disappearance of spirochaetes from surface lesions, (*b*) the healing of early lesions and (*c*) the reversal of a positive blood test in early syphilis. The order of decreasing efficiency in tests (*a*) and (*b*) is arsphenamine, silver arsphenamine, sulpharsphenamine and neo-arsphenamine. In test (*c*) the first three arsenicals named above are equally efficient and neo-arsphenamine is slightly less so

Mapharside by the same yardstick is, in adequate dosage, at least as efficient as neo-arsphenamine

Contra indications to Arsenical Therapy

There are a few instances when the arsenicals must not be used These are



NODULO-ULCERATIVE GUNDIA



NEOARSPHENAMINE

Ampoule on left is flawed, powder is discoloured and is unfit for use.
Ampoule on right shows normal colour of good neoarsphenamine

1 Old age, sixty years and over Arsenicals are dangerous and usually unnecessary
2 Major intolerance to arsenic.
3 Arsphenamine-resistant syphilis
4. Severe myocardial disease of any origin

Arsenicals, if used at all, are to be given with caution and only after preparatory treatment with mercury bismuth or both, in the following seven conditions, which have been described by Stokes as the seven bads

1 Bad brains and cords — acute meningeal and diffuse encephalitic processes, serious vascular involvement myelitis.
2 Bad livers — acute hepatitis, extensive late hepatitis and cirrhosis.
3 Bad spleens — cirrhotic splenomegaly
4. Bad vascular systems — myocarditis coronary lesions, aneurysm, febrile subacute bacterial endocarditis.
5 Bad lungs — advanced tuberculous and septic processes especially if febrile, acute bronchitis.
6. Bad kidneys — chronic nephrosis and nephritis
7 Bad skins — eczema, previous dermatitis, chronic urticaria.

Complications

The cause of complications may be found in the drug itself, in the solvent, in technique of administration or in the individual reaction of the patient. It is a good plan to note the batch number of the arsenical used so that if reactions occur in a number of different patients, the process of investigation is helped.

Toxic reactions do not always or even often mean that the arsenical treatment of syphilis must be discontinued The trouble may have arisen from some other source or a change of arsenical may solve the problem It must be remembered that the arsenicals are the most potent and certain weapons available for the cure of syphilis particularly in the early stages, and their use must not be discontinued without adequate reasons or because of lack of technical skill Careful technique, individual assessment and the use of the best drugs and solvents will minimize complications.

Reactions are far commoner after the trivalent than after the pentavalent arsenicals.

Local Reactions

Paravenous Injection. With the exception of sulpharsphenamine and Bismarsen, the injection of the drugs of the arsphenamine series into the tissues causes pain, inflammation and possibly necrosis

Accidental *paravenous injection causes pain and a burning* sensation at once, and if a patient complains during injection or if there is the slightest doubt felt by the operator the needle must be withdrawn and the injection given in another vein

The result of paravenous injection is a brawny indurated tender swelling which causes much discomfort and loss of function If a large amount of solution is extravasated necrosis of tissue may ensue. Abscess formation is rare and incision of the swelling is to be deplored unless it is certain that pus *is present*

Treatment of an established case is with hot fomentations. The patient is encouraged to move the arm as much as possible. The injection of saline, local anaesthetics or sodium thiosulphate is only likely to spread the irritant solution.

Pain in the Arm Cramping pain in the arm during injection occurs sometimes with arsphenamine and arsenoxide, and very rarely with silver arsphenamine and neo-arsphenamine. Rapid injection of arsenoxide avoids this minor complication.

Thrombophlebitis Closure of the veins by thrombosis is due in the case of original arsphenamine to improper preparation but this complication also arises when neo-arsphenamine or Stabilarsan is used It is fortunately a rare phenomenon for subsequent injections tend to produce the same result, and persistence may finally make intravenous injection impossible. The author considers this to be due to idiosyncrasy and an immediate change of arsenical is indicated.

The affected vein becomes hard and tender symptoms being noticed by the patient after twelve to twenty four hours. The vein feels like a cord rolling under the finger A sling should be prescribed for a week, but the danger of dislodging the thrombus *is remote.*

General Reactions

The general reactions can be roughly classified into im-

mediate, occurring at the time of injection delayed, occurring at some time after an individual injection and late occurring days or weeks after treatment and usually to be correlated to treatment rather than to an individual injection

Ether Smell One of the commonest symptoms resulting from the injection of arsphenamine, neo-arsphenamine and arsenoxide is a sensation of smell of ether or garlic. This appears while the intravenous injection is being made and is transitory and of no importance save in the rare instances when it apparently precipitates nausea or vomiting Holding the nose during injection is usually enough, or the patient can suck a peppermint.

Pulmonary Oedema and Embolism This is very rare and occurs during injection of acid arsphenamine or oxidized neo-arsphenamine. The patient at once becomes very ill and collapses Death may follow from pulmonary oedema or the patient may recover and present signs of localized pneumonia from emboli.

This is to be prevented by careful examination of ampoules and solutions before administration. Neo-arsphenamine must not be allowed to stand for long in solution before injection

Shock. A condition like surgical shock sometimes occurs immediately or a few hours after injection of an arsphenamine. Treatment is rest, warmth and, if necessary intravenous fluids

Acute Heart Failure The institution of arsphenamine therapy in cases of myocardial syphilis may precipitate acute heart failure by producing ventricular fibrillation The patient suddenly becomes pale, loses consciousness and often dies before anything can be done. If he recovers, arsphenamines are of course, contra indicated. This accident is avoided by proper examination of cases and by starting treatment gently with mercury and bismuth if there are signs of cardiac disease

Nitritoid Crisis This reaction is so named because of the similarity of the symptoms to those which follow the inhalation of amyl nitrite. It is a fairly common phenomenon is seldom dangerous and is not usually an indication for stopping arsenic. Arsenoxide is least likely to produce it. Nitritoid crisis may be immediate or delayed for a few minutes or hours. Rapid injection, save with arsenoxide, is a common cause.

The patient becomes suffused and his conjunctivae are

injected He complains of feeling hot, of pain in the chest and *of palpitation* He may choke and cough and produce an asthmatic attack, or he may vomit. The condition may go on to one of shock and consciousness may be lost Anglo-neurotic phenomena of swelling of face, lips eyelids or larynx, or urticaria may also be seen If any such symptoms appear injection must cease at once, but may be resumed very slowly if the attack quickly passes off If the symptoms are severe, a hypodermic injection of ½ c c 0·1 per cent adrenalin is *administered immediately and in the most serious cases* ½ c.c. adrenalin can be injected slowly into a vein Subsequent injections should be given very slowly and if the reaction occurs again it may be necessary to change to arsenoxide.

Hypodermic injections of adrenalin before the arsenic is given are sometimes effective. These reactions are seldom fatal and usually pass off in under half an hour

Delayed Reactions

In this category come delayed nitritoid crises like those already described and the tubing reaction which is confined to arsphenamine treatment and due to impurities in rubber tubing used in the apparatus Gastro-intestinal reactions are sometimes immediate but usually delayed

Gastro-intestinal Reactions Malaise, fever nausea, vomiting and diarrhoea may follow a few hours after injections and last for anything up to a few days The symptoms can be mini mized by seeing that the patient does not overload his stomach immediately before or after an injection and by avoiding constipation *Arsenoxide is rather less liable to cause this* reaction than is neo-arsphenamine

Febrile Reaction. A reaction characterized entirely by chills and fever coming on shortly after intravenous injection is generally due to impurities in the solvent Only sterile doubly or better trebly distilled water should be used

Jarisch-Herxheimer Reaction. Therapeutic shock, though not technically a true drug reaction is here recalled as it is most prominent after the arsenicals After the first arsenical injection secondary rashes may temporarily become more prominent. Dangerous reactions may arise if arsenicals are carelessly used without adequate *preparation in cardiovascular* syphilis or neurosyphilis

Late Reactions

The late complications of arsenical treatment can arise at any time from a few days to a few weeks after treatment. They are generally of much greater importance than the early reactions.

A Cutaneous

A very large variety of skin lesions can be encountered during arsenical treatment. Some of them are unimportant others are dangerous and give warning that arsenic must not in future be used Dermatitis is three times as common with the arsphenamine series as with arsenoxide. Sulpharsphenamine causes more dermatitis than any other arsphenamine. A patient who has had an arsenical dermatitis following arsphenamine treatment cannot, however be treated subsequently with arsenoxide.

Cutaneous tests for hypersensitivity to arsenic have been evolved but their results are ambiguous and they cannot be recommended either as aids to diagnosis or as guides to future treatment.

Urticaria and angio-neurotic oedema are usually associated with nitritoid crises and are treated with adrenalin injections

Herpes simplex and zoster may occur during arsenical treatment but their exact relation to the treatment is uncertain and arsenicals can be continued without fear

Ninth Day Erythema. This reaction, first described by Milian, consists of a diffuse erythema accompanied by malaise, fever nausea and vomiting and headache. It appears soon after the first arsenical injection, usually about the ninth day but may occur at any time between the fifth and nineteenth day

The phenomenon is usually seen in early syphilis, and Milian regarded it as an example of biotropism, for it occurs during the treatment of other diseases with arsenicals. Symptoms generally subside in two to six days and the patient should be confined to bed True arsenical dermatitis seldom develops directly from the original attack, but arsenic should be with held for a few weeks while treatment is continued with bismuth. After a lapse of three to four weeks arsenic can be resumed cautiously and it is wise to change the drug Mapharside or Neohalarsine can be tried if neo-arsphenamine was originally used (See also p. 283)

Dermatitis Macular maculo-papular papulo-vesicular vesicular and lichenoid eruptions are encountered as arsenical reactions. A dermatitis usually arises *fairly early in treatment*, after the first half-dozen injections but may begin earlier or later

The bends of the elbows neck, face and legs are usually the first sites, and blondes are more liable to attack than brunettes Patients should be examined for signs of cutaneous reaction before every injection

If signs of dermatitis appear arsenical treatment should be suspended until the condition subsides In the case of macular and maculo-papular eruptions Mapharside or Neo-halarsine can be tried in very small dosage (0·01 gm) afterwards, but vesicular or scaling eruptions are a danger signal and mean that trivalent arsenicals must never again be used. *Acetylarsan may be tolerated by such patients, but even this* must be tried out in minute doses at first

The great danger in cases of skin sensitivity is exfoliative dermatitis This may arise in fully developed form or may develop from a more localized dermatitis of any type, particularly if arsenical treatment is continued in spite of warning signs (Fig 83)

The patient is gravely ill and should always be treated in hospital. The skin is lobster red, shiny and oedematous. Later exfoliation of the surface epithelium begins and scales are shed. In the worst cases even the nails may fall off The face is swollen and the eyes closed Itching may be severe and weeping patches often develop Death can occur from exhaustion septicaemia *broncho-pneumonia or uraemia* The process of recovery is long and hazardous

Treatment of localized dermatitis is with calamine lotion or with a cream of zinc or calamine depending on whether the lesions are moist or dry Injections of sodium thiosulphate are often advised but they are probably useless. B.A.L. treatment, if available, is often most effective in all types of arsenical dermatitis (see p 267)

Cases of exfoliative dermatitis will only recover with constant careful individual nursing Frequent alkaline colloid oatmeal baths at a constant temperature of 98° F give excellent results provided the patient is fully immersed and not allowed to get chilled. Local applications of olive oil or



Fig. 83.—Exfoliative Dermatitis following Arsenical Treatment of Syphilis

glycerine pomades are made after the patient has been gently dabbed dry

After recovery from a severe dermatitis or exfoliative dermatitis, arsenic must never again be used and it is wise to mark the patient's documents clearly in red ink NO MORE ARSENIC EVER, and to advise him to refuse arsenical treatment if he goes to another doctor at any time.

Fixed Eruptions Patches of erythema which flare up in the same spot after each injection are sometimes seen. Continuation of treatment may produce an eczema or local pigmentation or rarely a generalized dermatitis. A change of arsenical and cautious procedure is advised

Miscellaneous Cutaneous Phenomena Arsenical pigmentation is extremely rare and occurs in cases having had prolonged treatment. Hyperkeratosis is also a rarity Pigmentation or vitiligo may follow exfoliative dermatitis. Argyria can follow the use of silver or neo-silver arsphenamine, but clinical evidence never appears until at least 8 gm. have been given.

Purpuric eruptions are considered with the blood dyscrasias, but their appearance, even in the mildest form, means that arsenic must not be used again.

B Blood Dyscrasias

Disorders of the haemopoietic system are commonest after sulpharsphenamine but may arise after treatment with any of the trivalent arsenicals. After any such accident treatment with arsenicals is absolutely contra indicated

Thrombocytopenia. In this condition purpuric skin eruptions and bleeding from the mucous membranes occur during or sometimes a few days after injection. A condition of shock may coincide. The platelet count is very low — down as low as 50 000 — but nothing else significant is found in the blood picture. Recovery is the rule with rest, but transfusion may occasionally be necessary if there is much haemorrhage Arsenical treatment must not be resumed.

Agranulocytosis The onset of sore throat, tenderness of the gums and fever is an indication for suspension of arsenic and a blood count Ulceration of the throat and mouth may appear and there may be a brawny oedema of the neck. Other complications such as jaundice, exfoliative dermatitis or purpura may co-exist There is often a very marked leucopenia with almost complete absence of granulocytes.

Treatment consists of injections of pentose nucleotide daily in doses of 10 to 20 c.c The intramuscular or intravenous route is chosen according to severity If a good response is forthcoming it will be evident clinically and in the blood picture by the fifth day The mortality rate has fallen from 90 to 25 per cent with this treatment.

Aplastic Anaemia The clinical and blood picture in this condition is a combination of the two previous conditions. There is fever purpura bleeding from mucous membranes, ulceration in the mouth and throat and sometimes jaundice or dermatitis. All the elements in the blood are affected and there is anaemia, leucopenia agranulocytosis and thrombocytopenia with no evidence of regeneration. If the patient can be tided over with blood transfusions until spontaneous marrow regeneration begins he may live Pentose nucleotide should also be used B.A.L. (see p 267) should be given in all cases of blood dyscrasia.

C Hepatic Complications

Hepatitis and jaundice as a complication of arsenical treatment is quite common in hospital practice, but in peace time is comparatively rare in private practice. As already described on page 186 a number of factors are involved. These include arsenic, syphilis, diet and an infective factor In times of economic depression the diet is inadequate in sulphydryl containing amino-acids necessary for the synthesis of glutathione the enzyme responsible for oxidation-reduction phenomena in the liver cells and for detoxication of arsenic. Low protein diet is potent in predisposing to hepatitis.

The hepatitis coincident with arsenical treatment usually occurs about the time of the eighth to fifteenth injection It is usually mild or moderate in character and indistinguishable clinically and pathologically from infective hepatitis Rarely subacute or acute yellow atrophy occurs

A high protein diet is protective, and arsenoxide is less liable to produce hepatitis than the arsphenamines Protection can also be afforded before or during the critical weeks by administering sulphydryl-containing amino-acids. This method of control is, as yet, not generally available.

Patients who develop jaundice should be treated with rest and a high protein and carbohydrate diet with eggs and milk, reinforced if possible with methionine or some other sulphydryl containing amino-acid. Sodium thiosulphate, often recommended is quite valueless

Arsenical treatment is suspended during the period of jaundice and for eight to twelve weeks after when it may be resumed Recurrence after resumption of arsenic is very rare but if there is any sign of intolerance, arsenoxide should be used Bismuth metal in doses of 0 4 gm. (2 c.c.) of the suspension in water should be given by intramuscular injection weekly throughout the course of the complication and in the ensuing weeks. Total suspension of anti-syphilis treatment will lead only to relapse of the syphilis

After a subacute yellow atrophy treatment should continue with bismuth only and arsenic is contra-indicated because a certain degree of residual cirrhosis is the rule.

D Renal Complications

Renal damage is rare with the arsenicals Albuminuria

in the course of treatment of syphilis will direct suspicion towards bismuth rather than arsenic. If stoppage of bismuth in such a case has no effect, the arsenical should be suspended for a time, and if it is to blame, the trouble will cease. After a short rest arsenic can be recommenced and seldom causes a recurrence.

A true nephritis can be associated with purpura and exfoliative dermatitis

E Haemorrhagic Encephalitis

This complication is fortunately rare. It occurs after the first three or four arsenical injections sulpharsphenamine and neo-arsphenamine being the chief offenders. Severe headache is followed by nervousness and then convulsions. Coma supervenes and death occurs in twelve to forty-eight hours. The onset is unpredictable and the only significant pathological change is an increase in the protein content of the cerebrospinal fluid. Only in the rapid treatment of syphilis is this complication likely to be encountered.

Treatment consists of spinal drainage by lumbar puncture, venesection, and repeated slow intravenous injections of 0·1 per cent adrenalin solution in ½ c c. doses. B.A.L. (see p 267) should also be used. Patients should be nursed in the sitting position. Recovery is exceptional.

F Peripheral Neuritis

Another very rare complication is toxic arsenical polyneuritis. Burning pains and numbness may be felt in hands or feet. Muscular wasting and even atrophy may result Sulpharsphenamine is usually responsible and the trouble begins late, after twenty or more injections but recovers on stopping treatment. Arsenic is contra-indicated in future

G Neuro-recurrence

This complication is not due to arsenicals but to their inadequate use. Incomplete arsenical treatment may partially subdue the spirochaetes and prevent the development of immunity Recurrence in the nervous system occurs in only 2 per cent of poorly treated early syphilitics, but manifestations are severe and include acute meningitis, hemiplegia and cranial nerve palsies The onset of symptoms is from one to nine



DEEP ICTERUS IN A PATIENT WITH HEPATITIS COINCIDENT WITH NEOARSPHENAMINE TREATMENT OF EARLY SYPHILIS



NORMAL URINE ON LEFT BILE-STAINED URINE ON RIGHT TEST TUBE SHOWS IODINE TEST FOR BILE IN URINE

PLATE VIII

months after cessation of arsenical treatment in early syphilis In such a case arsenical treatment at the heaviest tolerated dosage must be resumed at once.

COMPLICATIONS WITH PENTAVALENT ARSENICALS

Toxic phenomena are rare with the pentavalent arsenicals but mild cutaneous and hepatic reactions have been described Acetylarsan can often be used with safety in cases where arsenic is necessary but cannot be supported as a trivalent compound

The only dangerous phenomenon is visual injury which is encountered with tryparsamide and has been seen in a very few cases with Acetylarsan Signs of optic nerve injury are evident early in treatment and seldom appear after the twelfth injection. The patient complains of shimmering or cloudiness of vision and evidence of concentric contraction of the fields of vision is found At the least complaint of visual symptoms treatment must cease and should not be resumed, or complete optic atrophy and blindness may be the result. The visual fields should be charted before treatment starts and between courses.

If toxic reactions are quickly noted and treatment is stopped at once, no progression is likely to take place but recovery from the peripheral impairment is unlikely Optic atrophy due to neurosyphilis is usually but not always a contra indication to the use of tryparsamide. An existing optic atrophy increases the risk from tryparsamide tenfold

B.A.L. (O.X. • 7)

This compound has the property of causing rapid excretion of arsenic. Its use is indicated in those toxic conditions directly attributable to arsenic. The most impressive results are seen in cases of dermatitis, but it should also be given to patients with blood dyscrasias or haemorrhagic encephalitis.

The dosage now recommended is 8 c.c. (two ampoules) intramuscularly thrice daily for the first two days, then 4 c.c. twice daily to the end of a week.

Chapter XIX

TREATMENT OF SYPHILIS: PARTICULAR

EARLY SYPHILIS

A LARGE number of schemes of treatment for syphilis have been tested since the arsphenamines came into use. Out of the great mass of information available certain points stand out prominently

The best results are obtained by combining arsenical therapy with bismuth. It is now almost universally agreed that treatment should be continuous, without rest periods in which neither arsenic nor bismuth is given Overlapping allows of the necessary intermissions which avoid drug fastness and complications. The slightest deviation from the routine, particularly in the first three months, can be absolutely disastrous and the consequence may be the necessity for extensive prolongation of treatment.

The pathological tests indicated in the schemes of treatment are reduced to a bare minimum necessary for adequate control

The choice of bismuth preparation is simple An insoluble suspension of bismuth metal will normally be used. Arsenicals are chosen according to circumstance In the light of present knowledge, it will be best to use neo-arsphenamine for patients who can attend only once weekly and Mapharside or Neohalarsine for those who can attend twice weekly When intravenous therapy is utterly impossible sulpharsphenamine can be used This will not find favour with patients but is fairly effective though likely to produce toxic effects. If sulpharsphenamine causes great pain it is permissible to substitute Acetylarsan in the second and subsequent courses

Every case of early syphilis will therefore begin treatment with a *trivalent intravenous arsenical and bismuth, and* barring accidents will follow the routine shown on page 270

It is always wise to begin treatment with a relatively small dose of the chosen arsenical and to use intensive methods in the first few weeks

Blood tests are most valuable when taken after a rest from arsenicals.

Treatment after Complications

Resumption of arsenical treatment after complications such as hepatitis or ninth-day erythema should always be cautious and, if a drug of the arsphenamine series is used the initial dose should not exceed 0·15 gm All treatment must never be suspended in cases of toxic reactions. If arsenic is at fault, bismuth must be continued in higher dosage. When resumption of an arsphenamine is followed by signs of intolerance a change to arsenoxide is indicated, and if this is not found suitable, Acetylarsan can be tried.

After such complications the total amount of treatment should never be less than would normally be given, and may indeed have to be prolonged because the loss of the potent arsenical at a crucial time may delay the process of cure.

When a major complication such as dermatitis or blood dyscrasia necessitates total suspension of arsenical treatment at an early stage bismuth therapy must be continued over a period of at least two years This treatment should be continuous if possible, but if the bismuth is not well supported rest periods of one month can be interposed every three or four months. Mercury and iodides are prescribed during such rest periods

LATE SYPHILIS

There can be no rigid schedule of treatment applicable to all cases of late syphilis for the widest clinical variations are encountered each type requiring special consideration In cases of apparent latency in young people the scheme of treatment outlined for early syphilis should be applied A diagnosis of latency will depend on repeated positive blood tests and an absence of all physical signs of disease in the presence of negative findings in the cerebrospinal fluid

Before starting treatment in any case of late syphilis, the condition of the viscera must be estimated as accurately as possible so that the therapeutic measures may be graduated to coincide with the clinical state. The possibility of therapeutic shock, which can be dangerous and even fatal, must not be forgotten. Patients with late syphilis are usually older than those with early syphilis.

For these reasons intensive therapy is contra-indicated and

SCHEME OF TREATMENT FOR EARLY SYPHILIS

Weeks	Day	Neo-arsphenamine (or [illegible])	Bismuth Aqueous Suspension	Alternatives to Neo-arsphenamine: Mapharside	Sulpharsphenamine	
		gm.	gm.			
		0·30	0·2	gm.		
	4	0·45		0·04	gm.	
	7	0·45		0·06	0·3	W.R. and Kahn test.
2			0·2		0·45	
	1[1]	0·45		0·06		
				0·06	0·45	
3	4	0·45				
	8		0·2	0·06		
		0·45				
4	25	6		0·06	0·45	
			0·2			In this scheme course lasts 4 weeks. A typical course is shown in weeks 15 to 28. The first 14 weeks are atypical because of the necessary intensive start. Blood tests are always taken at the end of rest from arsenical treatment. The average healthy young woman will receive the dosage shown here. Do not reduce dose for women below 0·45 gm. neo-arsphenamine or its equivalent. Test urine for albumin and, if possible, for urobilinogen before each injection. Weigh the patient each week.
5		0·6		06 twice weekly		
6			0·2	0·06	0·45	
7		0·6	0·2	0·06	0·45	
8		0·6	0·2	0·06	0·45	
9		6		06	0·45	
		0 6	0·2	0·06 "	0·45	
		6	0·2	06	0·45	
2			0·4		0·45	
3			0·4			
4			0·4			
			0·4			
15						
6		45				
		6		0·06 twice weekly		
17		0·6		0 06	0·45	W R. and Kahn test.
				0·06	0·45	Lumbar puncture about this time in cases of sero-positive primary syphilis or secondary syphilis.
8					0·45	
		0·6				
9–24		6 per week		0·06		
5–28			0·2 per week	0·06	0·45	
29			0·4 "		0·45 per week	
		0·45		0·06 "	0·45	W.R. and Kahn test.

30–32		0·6 per week	0·4 per week	0·08 twice weekly	0·45 per week	
33–38		0·6	0·4 „	0·06 „	0·45 „	
39–41		45		06	0·45	W.R. and Kahn test.
43		0·6 per week		0·06 once weekly	0·45 per week	Treatment ceases here in cases of sero-negative primary syphilis. Observation period begins.
44–46		6	0·4 per week	0·06 „	0·45 „	
47–51						

If neohalarsine is the chosen arsenoxide, the first dose is 0·06 gm., and subsequent doses 09 gm. twice weekly

Sero-negative primary syphilis has four courses as shown above, provided the blood tests remain negative throughout.

Sero-positive primary and secondary syphilis is treated on the above scheme until blood tests are negative, and then further three courses are given. A negative blood test is usually obtained in such cases at the 5th week, in which case treatment will theoretically be the same as for primary sero-negative case.

OBSERVATION AFTER TREATMENT FOR EARLY SYPHILIS

Months after treatment ceases			
3	W.R. and Kahn Test	Lumbar Puncture	
6, 9, and 12	„ „		
18	„		
24	„	Lumbar Puncture	X-ray of Chest

At every visit the patient must be completely examined as to condition of the skin and mucous membranes, cardiovascular and nervous systems. The radiological appearance of the heart and aorta should always be discovered at the last visit. Any doubtful or positive blood test result must be confirmed by repetition at once. Doubtful results must not be dismissed as irrelevant. Treatment must be resumed t once if clinical or serological relapse occurs.

If all the above tests are negative after adequate and uninterrupted treatment, the patient may resume normal life or marry and have children.

Women, whether pparently cured or not, must have treatment during every pregnancy

All patients are advised to have general overhaul and blood test every five years for the rest of their lives.

the arsenicals are less prominent in the treatment of late syphilis and are not used until the patient has been suitably prepared Arsenicals are seldom given to patients over the age of sixty

The scheme of treatment shown for late syphilis is applicable in any case where there is no gross visceral involvement for example, in late cutaneous or osseous syphilis (p 273)

Sero resistance

This subject can suitably be considered at this time because reversal of positive blood tests is generally more difficult in late than in early syphilis. In early syphilis a positive blood test will usually be reversed to negative by one or at most, two courses of treatment, but occasionally cases will be encountered in which reversal is delayed Such cases must be watched *carefully for evidence of relapse or retrogression* and *lumbar* puncture is always indicated. Treatment must be continued until a negative test is obtained and for a year afterwards A rest from arsenicals for three months is indicated after the fifth course if prolonged treatment is necessary

In late syphilis sero-resistance is not quite so important and indeed, after cessation of treatment, reversal may eventually occur spontaneously A change of therapy can sometimes effect serological reversal.

The important point in sero-resistance is to ensure that treatment is continuous, adequate and uninterrupted In early syphilis this same principle will avoid the complications. Relapse is commoner with sero-resistance than when reversal occurs easily

In sero-resistant as in any other cases of syphilis, a fundamental is to remember that it is the patient who is to be treated and not the blood test

NEUROSYPHILIS

Neurosyphilis can be avoided by adequate continuous treatment of early syphilis with arsphenamines and bismuth. No rest periods should be given and defaulters must be vigorously pursued.

The results of treatment must be controlled in all cases, no matter what the stage of disease, by repeated examinations of the cerebrospinal fluid

SCHEME OF TREATMENT FOR LATE SYPHILIS

Weeks	Bismuth (Aqueous suspension)	Neo-arsphenamine		
	0·4 gm. per week		Mist. Hydrarg. Iodidi t.d.s. W.R. and Kahn test	This can also be given between courses of arsenic.
3		0·3 gm.		Arsenoxide can be substituted for neo-arsphenamine.
4		·30		0·3 neo= 0·02 Mapharside or 0·03 Neohalarsine.
5		0·45		0·3 ,, = 0·04 ,, ,, 0·06 ,,
6		·60		0·45 ,, = 0·06 ,, 0·09 ,,
17–22	0·4 per week	·60 per week		Bi-weekly injections of the chosen arsenoxide should be given from the 6th until at least the 96th week. The dose should not exceed ·06 gm. Mapharside or ·09 gm. Neohalarsine.
23–26	0·4			
27		0·45	W.R. and Kahn test	This scheme of treatment is applicable in all cases of late syphilis without gross visceral damage.
28–30		·60		
31–36	0·4 per week	·60 per week		
37–40	0·4			Test urine for albumin and, if possible for urobilinogen before each injection.
4[illegible]		0·45	W.R. and Kahn test	
42–44		·60 per week		
45–50	0·4 per week	0·60 ,,		
51–54	0·4		W.R. and Kahn test	
55		0·45		
56–58		0·60 per week		
59–64	0·4 per week	0·60 ,,		
65–76			Rest from treatment W.R. and Kahn test Lumbar puncture Review of case	
77				
78	0·4	0·45		
79–87	0·4 per week	·60 per week		
88–99			Rest from treatment W.R. and Kahn test Review of case	
100				
1[illegible]	0·4 per week			

If blood test positive, give neo-arsphenamine, as in weeks 78 to 87. Patient is now examined and has blood tests every three months. If blood tests remain positive ten-week course of bismuth, 0·4 gm. per week, is given once each year. Lumbar puncture is repeated two years after cessation of actual arsenical treatment. Observation continues at yearly intervals.

Early Neurosyphilis

In cases where the symptomatology and pathological findings indicate that the process is predominantly meningeal treatment should be on the lines laid down for early syphilis. Lumbar puncture should be repeated every six months.

When there is evidence of vascular involvement as in transverse myelitis, preparatory treatment with iodides in large doses by mouth or intravenously and bismuth is necessary to avoid therapeutic shock. In such cases the scheme suggested for late syphilis is applicable, but a soluble bismuth preparation such as Thiobismol should be used twice weekly in the early stages.

Treatment in early neurosyphilis should continue for a year after the cerebrospinal fluid returns to normal

Parenchymatous Neurosyphilis

General paralytics are best treated by fever therapy with malaria, followed by prolonged treatment with tryparsamide. The general principles are discussed on page 948. Cases of primary optic atrophy also benefit by this type of treatment Malarial therapy is also used sometimes in very resistant cases of tabes dorsalis, but results are not striking in this condition.

Tryparsamide is the drug of choice in tabes dorsalis and in *other cases of neurosyphilis resistant to treatment by arsphenammes* A check is kept on the visual fields before and during treatment and tryparsamide is stopped at once if any visual disturbance is noted Bismuth is administered at the same time.

Courses of treatment last ten weeks and consist of one weekly injection of 3 gm of tryparsamide and one of 0·4 gm of bismuth (for example, bismostab) Treatment must be prolonged for years if necessary and evidence of response may not be apparent for months. Tryparsamide has a marked tonic effect and may restore lost sexual power *The arsphenamines* and arsenoxide are also used in tabes dorsalis.

Subdural treatment is recommended by J E. Moore (*Modern Treatment of Syphilis*) in some cases of tabes dorsalis and optic atrophy The patient's own inactivated serum or his own cerebrospinal fluid, *reinforced with arsphenamine*, is introduced by lumbar or cisternal puncture.

Symptomatic treatment is important in tabes dorsalis. Ataxia can be helped by remedial exercises and re-education. Charcot's joints and perforating ulcers can often be improved by the orthopaedic surgeon and bladder complaints by the urologist.

For lightning pains and gastric or other crises which persist in spite of active treatment sedatives are necessary Veganin and large doses of bromide can be used, but morphia should be withheld except in extreme cases, lest a habit be formed

Recently vitamin B (thiamin chloride) has been reported as giving good results. J E. Moore advises daily injections of 100 mgm for seven to ten days and 50 to 100 mgm. weekly thereafter

CARDIOVASCULAR SYPHILIS

General treatment of the essential cardiac condition must not be forgotten in handling syphilis of the cardiovascular system. Rest and a regime suitable for the patient s capabilities must be planned Good early treatment will reduce the incidence of these complications, and careful investigation after the cessation of treatment will reveal early cardiovascular changes in time for them to be successfully tackled

Early cases of aortitis, discovered before gross clinical signs appear can be treated on the plan shown for late syphilis. Bed rest is advisable though not essential in the early stages but when arsenical treatment begins the patient should be at rest and under observation until it is evident that the danger of therapeutic shock has passed.

With aortic valvular disease or aneurysm a preparatory period of two months on Mist Hydrarg Iodidi (Pot. Iod 10 grains rising to 60 grains) thrice daily should precede the routine for late syphilis. Here again rest is advised in the early stages and later when the arsenicals begin

When there is evidence of myocardial degeneration, or in old people arsenic should be withheld Mercury and iodides for two months precedes bismuth treatment, which is given in ten-week courses of 0·4 gm. of aqueous metallic suspension weekly Rests of four to six weeks on mercury and iodides are given between courses, and treatment must be prolonged for two years or more.

When there is heart failure only Mist Hydrarg Iodidi is

given, together with the routine treatment by digitalis, etc., until compensation is regained Bismuth treatment can then begin and at the end of three months if the patient's condition is good arsenicals can be tried The initial dose should not exceed 0·05 gm. neo-arsphenamine or 0·005 gm. Mapharside, and the eventual highest dosage must not be above 0·3 gm. neo-arsphenamine or 0·03 gm. Mapharside. The lines of the scheme for late syphilis can then be followed.

Therapeutic shock is avoided if cases of cardiovascular syphilis are brought gently under treatment. Therapeutic paradox may be encountered in cardiovascular syphilis. A patient may at first improve on treatment and then produce such signs as heart failure or accentuation of valvular incompetence. *This paradox is due to dilatation of the aorta, as the* process of repair begins in the diseased and degenerate wall. This is another reason why rest is important in treatment Such phenomena need not be viewed too gravely provided due care is taken for if adequate treatment continues, the disease process is arrested and there is no further progression Therefore, although the signs may be more obvious, the ultimate prognosis is better

Progress is checked in cases of cardiovascular syphilis by repeated radiological examinations and by electrocardiography

The possibility of coincident neurosyphilis should always be considered and lumbar puncture is indicated in all except the gravest cases Tryparsamide can be given without danger even when trivalent arsenicals are contra indicated

VISCERAL SYPHILIS

Late syphilis of the skin, bones intestines and testes can be treated by the scheme laid down for late syphilis generally for there is no danger of therapeutic shock.

Respiratory Tract In gummatous conditions of the larynx and trachea a month's preparation with iodides should precede the scheme for late syphilis so that oedema of the larynx as a Jarisch-Herxheimer reaction may be avoided

Kidney If a syphilitic nephritis is suspected treatment should be with small doses of neo-arsphenamine or arsenoxide without heavy metals which are themselves nephrotoxic

Liver and Spleen The rare cases of hepatitis associated with

early syphilis or occurring as relapse phenomena can be treated with arsphenamines without danger but dosage should be reduced to half the scale shown in the early treatment scheme until resolution is complete.

In late syphilis of the liver preparation with mercury and iodides for a month must precede bismuth therapy on the lines laid down in the treatment of cardiovascular syphilis.

Arsenicals are generally contra indicated in late hepatic syphilis, but may sometimes be used in cases of gummata after long preparation.

Therapeutic paradox is sometimes seen when after a few weeks of treatment an initial improvement gives way to relapse and ascites Therapeutic shock or paradox are both likely with arsenicals

When jaundice is present general treatment should include a high protein and carbohydrate diet. Ascites is a sign of the worst prognostic significance. If ascites appears, tapping should be avoided until it is evident that other measures, such as fluid restriction cathartics and mercurial diuretics, have failed Once tapping has started it usually has to be repeated frequently until the patient's death. Omentopexy has occasionally been successful in chronic ascites

In cases of splenomegaly without evidence of gross hepatic damage the scheme for late syphilis can be used.

The Eye Apart from optic atrophy the treatment of syphilitic ocular conditions should be energetic and on the lines laid down for early syphilis. There is no danger of therapeutic shock.

The best treatment for optic atrophy appears to be malarial therapy followed by treatment with trivalent arsenic and bismuth, as in the late syphilis schedule. Tryparsamide is best avoided. Subdural therapy has sometimes given good results, but fever is preferred.

Treatment of Pregnant Women

A blood test should be routine in every woman when she comes under antenatal care. Repeated positive blood tests are concrete evidence of syphilis and there is no truth in the theory that pregnancy alone can produce a positive serology

A woman with untreated or partially treated early or latent syphilis has only about one chance in six of producing a healthy

child. If antisyphilitic treatment is started before the fifth month of pregnancy the chances of a healthy child are excellent.

The scheme of treatment in pregnancy is essentially that of early syphilis and full doses of neo-arsphenamine or arsenoxide (twice weekly) should be given as soon as a diagnosis is made. The courses should be planned so that the arsenical is being administered during the last month. If the diagnosis is not made until the sixth month or later continuous treatment with arsenic and bismuth should be given in full doses and without rest periods until the end

Treatment of the mother should continue without interruption after the child is born, the previous treatment having been directed at the foetus Four full courses are given after the birth or after the first negative blood test subsequently All the usual routine tests are performed.

If a woman who has had syphilis becomes pregnant after treatment is complete, it is considered wise to resume treatment on the above lines during this and subsequent pregnancies.

Minor toxic phenomena are to be ignored, and the risk of major treatment complications is not markedly increased by pregnancy

The child of a syphilitic mother should always be bottle-fed from the start

The child of a syphilitic mother should not be treated immediately unless it shows clinical signs of congenital syphilis. The child should have blood tests repeated fortnightly over three months. An originally positive test reverting to negative indicates a healthy child, as does a persistently negative test. A persistently positive test or an early negative reverting to positive means that treatment must begin whether there is clinical evidence of disease or not

Therapeutic abortion is not indicated as the results of energetic treatment are satisfactory

CONGENITAL SYPHILIS

Early Congenital Syphilis

Early congenital syphilis should be energetically treated, like early acquired syphilis with arsenic and bismuth. A number of arsenicals have been tried in the past but a survey

of recent opinion indicates a general preponderance in favour of sulpharsphenamine.

Acetylarsan is also a reliable drug but has the disadvantage that bi weekly injection is essential for good results Acetarsol is uncertain in its effects Its use should be confined to hospital practice, because the average parent of a congenital syphilitic child cannot be relied upon to give regular dosage. With adequate dosage toxic effects are very common. Mercury like acetarsol is best avoided as a very poor remedy

A reliable scheme of treatment modelled on a plan suggested by J E. Moore (*Modern Treatment of Syphilis*) is shown in tabular form on page 280

Acetylarsan. If acetylarsan is used it can be substituted for sulpharsphenamine in the scheme of treatment, dosage being calculated according to the following table

ACETYLARSAN DOSAGE TABLE FOR CHILDREN

Weight of the Child in lb.	Weight of the Child in kilos	First Injection, c.c.	Rest Period	Second Injection	Rest Period	Third and Following Injections	Rest Period	Solution to be used
6–9	3–4	0·2	3–4 days	0·3	3–4 days	0·5	One week	Acetylarsan (children)
10–14	5–6	0·3		0·5		0·7		
15–18	7–8	0·4		0·7		1·0		
19–22	9–10	0·5		1·0		1·3		
23–27	11–12	0·6		1·2		1·7		
28–33	13–15	0·7		1·5		2·0		
33–40	16–18	0·3	3–4 days	0·6	3–4 days	1·0	One week	Acetylarsan (adult)
41–49	19–22	0·4		0·8		1·2		
50–58	23–26	0·5		1·0		1·5		
59–66	27–30	0·6		1·2		2·0		

Acetylarsan may sometimes be preferred if infants are very much upset by pain from sulpharsphenamine or after toxic reactions.

Acetarsol If oral administration has to be used, acetarsol can best be given according to the Bratusch-Marrain scheme shown below

1st week, 0·005 gm. per kilo body weight daily
2nd week, 0·01 gm. " " " "
3rd week, 0·015 gm. " " "
4th to 9th week, 0·02 gm. per kilo body weight daily
10th to 13th, rest period with blood test at the end

TREATMENT OF EARLY CONGENITAL SYPHILIS

Weeks	Drug	Dose		
1	Sulpharsphenamine	5– mgm. per kilo	Blood test	
	Bismuth	0·05 gm.		An aqueous suspension of bismuth metal is used
2–7	Sulpharsphenamine	5 mgm. per kilo		0·05 gm. = ½ c.c.
	Bismuth	0·05 gm.		
8–	Bismuth	05 gm.		1 kilo = 2·2 lb.
[illegible]– 9	Sulpharsphenamine	5 mgm. per kilo	Blood test	
10–25	Bismuth	0·05 gm.		
26–33	Sulpharsphenamine	25 mgm. per kilo	Blood test	
34–[illegible]	Bismuth	0·05 gm.		
42–49	Sulpharsphenamine	5 mgm. per kilo	Blood test	Lumbar puncture
50–59	Bismuth	0·05 gm.		

This is the minimum of treatment. Alternating courses of arsenic and bismuth are to be continued until three of each has been given after the blood test has become permanently negative.

Thereafter observation continues six-monthly for an indefinite period and yearly course of ten weekly injections of 0·2 gm. bismuth should be given until puberty at least.

Patients with persistently positive blood tests should be seen frequently and course of bismuth every six months is advised.

Courses are repeated until blood tests have been negative on three successive occasions. After a rest of six months another course is given.

Mercury Inunctions of 1 gm of Ung Hydrarg daily are sometimes combined with acetarsol treatment in puny infants in the early weeks. Mercury by mouth is grossly inefficient and bismuth is much superior for intramuscular injection.

Late Congenital Syphilis

Late congenital syphilis is treated on the same general lines as late acquired syphilis and the routine of treatment is identical Dosage is modified according to age. Intravenous arsenicals should be used if possible. Up to the age of twelve years the dose of neo-arsphenamine should not exceed 0·3 gm and between twelve and sixteen years should not exceed 0·45 gm. Adult dosage is used after sixteen years.

When the full scale of treatment has been given the patient should have a ten weeks course of bismuth (0·4 gm. aqueous metallic suspension per week) each year thereafter If the blood test remains positive, courses should be given every six months. This treatment is given mainly as a precaution against interstitial keratitis. Neurosyphilis and other visceral complications are treated by the same methods as are used in the acquired types.

Interstitial keratitis requires the most energetic treatment as soon as it is diagnosed, and the scheme for early acquired syphilis should be used, dosage being modified according to the age of the patient. Atropine and hot bathing are useful in the acute phase. Fever therapy with T.A.B. vaccine gives very good results when combined with arsenotherapy The fevers should be induced on days following arsenical injections and from three to seven treatments are given Iodides are contra-indicated in interstitial keratitis. In cases where there is scarring and vascularization of the cornea, improvement continues slowly under treatment for as long as two years

In all cases of late congenital syphilis it is wise to give a ten weeks' course of bismuth each year after the active phase of treatment has ceased. Plastic surgery for facial deformities can be attempted after treatment is well under way

MASSIVE ARSENOTHERAPY

The standard treatment of syphilis with arsenic and bismuth is effective only if patients will attend with great regularity over a long time. Even under Service conditions of discipline at best only about 50 per cent of patients with early syphilis received, by this method, what can be considered adequate treatment. In order to offset this tendency to default and to cater for certain people, for example merchant seamen, who are unable to get regular treatment, many attempts were made to evolve a rapidly effective method of arsenotherapy

Success was never attained until the demonstration that speed shock due to rapid intravenous injection of certain drugs, could be avoided by using a slow intravenous drip This discovery was applied to early syphilis in 1934 when Chargin and others, in New York, treated patients with early syphilis with 4 gm. (later raised to 5 gm.) neo-arsphenamine given by slow continuous intravenous drip over four to five days. Toxic effects were frequent and there was an alarming fatality rate of 1 in 111 cases from haemorrhagic encephalitis. Neo-arsphenamine was therefore abandoned.

Mapharside was next tried and the optimum dose was found to be 1200 mgm. given at a rate of 240 mgm. a day in 2400 c.c. of 5 per cent dextrose solution It was soon found that the technique could be simplified without loss of efficiency by giving the same total in divided doses by syringe injections four times daily over five days. The fatality rate from haemorrhagic encephalitis was less, but still very high at 1 in 300 cases treated. About 85 per cent of patients treated with neo-arsphenamine and 82 per cent of those treated with Mapharside were clinically and serologically negative at follow up varying between six months and six years later

Haemorrhagic encephalitis is believed to be precipitated by the accumulation of arsenic in the tissues. In order to achieve equally good results in greater safety combinations of pyretotherapy with smaller doses of Mapharside were used Fever increases the potency of arsenic by assisting its penetration into tissue, and high fever in itself has a spirochaeticidal action. In one method fever was induced by typhoid vaccine four times in an eight-day treatment. In another Mapharside

was administered during a single ten-hour session of high fever at 160 F

The experimental work of Eagle and Hogan has shown that, within limits, the curative dose of Mapharside is independent of the time period over which the treatment is given Continuous drip methods are less effective than repeated injections giving the same total dose over the same time. On any dosage schedule the shorter the time in which the total dose is administered the lower is the margin of safety with regard to toxic effects. From this basis a number of treatment schedules have been formulated and tested.

One of the safest and most successful methods is the twenty-day treatment In this a total dose of 20 mgm Mapharside (or 30 mgm Neohalarsine) per kilogram body weight (*e.g.* 1200 mgm. for a 60-kg man) is administered by twenty equal daily injections (each of 60 mgm. in the example chosen) Bismuth injections at the rate of two a week during the treatment period enhance the results. This method was used extensively in the Allied forces before the advent of penicillin with results as good as those attained by long term methods (allowing for default, etc.) and with an even lower fatality rate. The twenty-day treatment like the other rapid methods described above, requires that the patient be hospitalized. During treatment the temperature must be taken at least twice daily the urine tested for albumin and urobilinogen daily and a total and differential white cell count done twice weekly

The major risks in the treatment are haemorrhagic encephalitis and blood dyscrasias, both of which are, to a large extent, unpredictable. Hepatitis during treatment is rare and always mild, but this complication may arise after treatment (60–100 days later) when it is probably due to the introduction of an infective (virus) factor during the period of injections. Toxicodermal reaction (ninth-day erythema) is fairly common occurring between the sixth and fifteenth days, with fever malaise, and erythematous eruptions. This is sometimes the precursor of some major toxic effect and means that treatment must be stopped When the reaction has subsided and the temperature has been normal for 48 hours it is sometimes possible to desensitize the patient by giving daily small and gradually increasing doses of Mapharside ($\frac{1}{100}$th, $\frac{1}{50}$th $\frac{1}{20}$th

of the original daily dose, etc.) continuing until the required total dose has been given

A modified intensive treatment suitable for out patients consists in the administration of 60 mgm. Mapharside three times a week for ten weeks. Bismuth is used concurrently

Another semi-intensive treatment, lasting 26 weeks, consists in two ten-week courses of Mapharside in 60-mgm. doses given twice weekly Bismuth is given once weekly in the first five weeks, in a six week rest between the courses of arsenic, and in the last five weeks of treatment.

The rapid treatment of syphilis (in 30 days or under) always requires hospitalization of patients and its use is contra indicated unless the physician and the nurses employed have received special training in the method Even the ten week course described above has hazards well above the average for long term treatment. Intensive methods have no place in the *treatment of late syphilis.*

The advent of penicillin has enormously reduced the use of rapid arsenotherapy but the two can be combined to advantage, and a combination with arsenic in reduced dosage (and consequently fewer toxic effects) gives very *satisfactory results.*

Rapid treatment was most essential in war time to conserve man power in spite of the increased possibility (which did not materialize) of major toxic effects. The need is less in peace and indeed very few patients would or could submit to hospitalization, but the aim in syphilis must always be towards reduction in time of treatment so that cure may be effected *before the patient begins to default.* Penicillin combined with a modified form of rapid arsenotherapy and bismuth seems the line of investigation likely to be most profitable in this pursuit.

CHAPTER XX

PENICILLIN TREATMENT OF SYPHILIS

PENICILLIN has already been shown to be an efficient spirochaeticidal agent and to be useful in the treatment of syphilis at all stages. It has an enormous advantage over all previous remedies for syphilis in that it is non toxic and free of any risk of death or major catastrophe (therapeutic shock excluded, and even this is not directly attributable to penicillin) Penicillin bids fair to oust arsenic from pride of place as the most powerful remedy against syphilis. Early over-enthusiasm has been tempered by experience, and it is now recognized that penicillin is not alone, at least by methods now used the answer to the problems of syphilis. If a satisfactory method of using penicillin alone could be found, the treatment of syphilis would become very simple. No single remedy in the past has been entirely satisfactory and, considering the infinite variability of syphilis, it would be remarkable if penicillin was the exception.

Penicillin ought to be used as a method of attack in every case of early syphilis, and it has been demonstrated to be useful, in varying percentages of cases, at all stages. Its contra indications are few and will be discussed later The effects of penicillin appear to be enhanced by its combination with other remedies, in particular arsenicals.

Research into treatment methods for syphilis has suffered in the past from shortage of supplies and because the venereal diseases usually figured last on any list of allocations for experimental projects. The treatment schedules shown here are to be considered as interim suggestions and liable to be amended in the light of future experiments. No scheme of penicillin treatment will suffer by increasing the amount of individual doses or by lengthening the treatment period, and future trends are likely to be in this direction

Some general points are (1) the earlier treatment begins the better the results with penicillin or any other remedy (2) results in patients treated with aqueous solutions of penicillin are better than in those treated with oil-wax suspensions,

of the original daily dose, etc.) continuing until the required total dose has been given.

A modified intensive treatment suitable for out patients consists in the administration of 60 mgm Mapharside three times a week for ten weeks. Bismuth is used concurrently

Another semi-intensive treatment, lasting 26 weeks, consists in two ten week courses of Mapharside in 60-mgm doses given twice weekly Bismuth is given once weekly in the first five weeks, in a six week rest between the courses of arsenic, and in the last five weeks of treatment.

The rapid treatment of syphilis (in 90 days or under) always requires hospitalization of patients and its use is contra indicated unless the physician and the nurses employed have received special training in the method Even the ten week course described above has hazards well above the average for long term treatment. Intensive methods have no place in the treatment of late syphilis.

The advent of penicillin has enormously reduced the use of rapid arsenotherapy but the two can be combined to advantage, and a combination, with arsenic in reduced dosage (and consequently fewer toxic effects) gives very satisfactory results.

Rapid treatment was most essential in war time to conserve man power in spite of the increased possibility (which did not materialize) of major toxic effects The need is less in peace, and indeed very few patients would or could submit to hospitalization but the aim in syphilis must always be towards reduction in time of treatment so that cure may be effected before the patient begins to default. Penicillin combined with a modified form of rapid arsenotherapy and bismuth seems the line of investigation likely to be most profitable in this pursuit.

long enough to allow of accurate appraisal of results. There is reason to believe that, up to a point, increasing the dosage of penicillin will increase the number of cures

Treatment Failure

Relapse or failure after treatment with penicillin may be manifested in a variety of ways. Failure, fortunately can usually be diagnosed within a few months after treatment and cases can be treated again by more energetic methods without any great harm being done. Careful clinical examination is most essential at the follow up visits of patients treated by any rapid method. The forms in which failure may occur are

(*a*) *Surface Relapse* Cases are sometimes seen where the chancre fails to heal completely and later breaks down again. Oftener the chancre heals completely but, after a latent period, reappears on the original site and may then be accompanied by signs of secondary syphilis. Sometimes relapse phenomena are entirely secondary in type the primary lesion remaining healed Evidence of serological relapse often but not always, precedes or accompanies surface relapse.

Relapse lesions are often small and discrete and may escape notice by the patient. The ano-genital area should always be inspected closely at routine follow up examinations as it is a common site for relapse phenomena of the condylomatous type.

(*b*) *Serological Relapse* In successfully treated cases of early syphilis, positive serum tests reverse to negative in 2–5 months. Serological relapse is diagnosed when serial quantitative serum tests show an increasing titre of positivity following a phase of negativity or declining positivity

(*c*) *Sero-resistance* This state is diagnosed at the end of an arbitrary period of 6 months in cases where serial tests have shown a maintained level of positivity In some cases there is no decline after treatment in others there is a decline to a lower maintained level.

(*d*) The less common relapse phenomena include neuro-recurrence, ocular and osseous relapse, and persistence of *S pallida* in surface lesions in spite of treatment.

Combined Treatment

The failure rate in patients with early syphilis treated with penicillin alone (2,400 00 units) in the British Army was high

enough soon to make the author dissatisfied Penicillin was then in short supply (1944–5) and the most profitable line of research appeared to me to lie in using combinations of arsenical and penicillin treatment. Experimental series in America had shown that there was apparently a synergistic action when the two drugs were used together Penicillin in small dosage (60 000 to 300 000 units) when combined with Mapharside (8 daily doses of 40 mgm.) gave results as good as those obtained with 1 200 000 units penicillin alone. Dr F R. Selbie, from his work on *S pallida* infections in rabbits, advised the author that the dosage of arsenic to be used with penicillin should for safety be not less than one half of the dose normally used by itself, in the treatment of any particular type of syphilis.

As a rapid treatment was essential in Service conditions, the scheme the author eventually adopted was a combination of 2,400 000 units penicillin *(given over 7½ days) with arsenoxide* (Mapharside 60 mgm or Neohalarsine 90 mgm.) in daily injections for ten days. The results with this treatment were better than those with penicillin alone, but the method carried a certain hazard of arsenical toxic effects (much less, however than with the twenty-day arsenoxide method)

The results of this experiment, and of similar schemes used by other observers, have made the author recommend for general use at the present time treatment schedules in which penicillin is used as a treatment of attack, and consolidation (and possibly synergistic effect) is maintained with arsenic and bismuth Rapid methods are not detailed as they are inappropriate for general use.

TREATMENT SCHEDULES

Primary Sero-negative Syphilis

The aim should be to start arsenical and penicillin therapy at once, but, if this is not feasible, treatment with arsenic and bismuth should begin immediately after diagnosis, and penicillin superimposed as soon as possible.

Arsenic and bismuth A ten week course is given, consisting of bi-weekly injections of arsenoxide (0·06 gm. Mapharside or 0·09 gm. Neohalarsine) and one weekly injection of 0·2 gm. bismuth metal suspension (*e.g* Bismostab) This is the treatment of election but if the patient can attend only once weekly neo-arsphenamine is the arsenical of choice, given in dosage of

0·45 gm. twice in the first week, and then 0·6 gm. weekly for nine more weeks.

Penicillin If possible, patients should be admitted to hospital to receive 3,000 000 units penicillin in aqueous solution given in sixty injections, each of 50 000 units 3 hourly over 7½ days. When treatment can begin with all these agents at once, so much the better

Penicillin in oil wax suspension is used for ambulant patients. One injection of 300 000 units is given each day for ten days.

No possible harm can be done by exceeding the doses of penicillin suggested above.

Primary Sero-positive and Secondary Syphilis

Treatment as above is given in the first ten weeks. In weeks 11–14 treatment continues with one weekly injection of bismuth. Blood is taken for testing at the 14th week. In weeks 15–24 arsenoxide is given bi-weekly and bismuth is continued once weekly in weeks 19–24.

Follow-up Patients should attend for examination and blood tests one, three and six months after treatment. An examination of the cerebrospinal fluid should also be made six months after treatment to exclude early neuro-recurrence. If positive blood tests have by this time reverted completely to negative, and there are no signs of surface relapse on skin or mucous membranes, observation should then continue once every three months for a year and then once every six months for yet another year The cerebrospinal fluid must be examined at the time of the last test above.

If all these tests are negative the possibility of future relapse is negligible, but in the interests of safety and considering the limitations of our knowledge of penicillin, it is advisable to see patients and repeat blood tests once each year for three more years.

Re-treatment of Failures In any case where failure is diagnosed, and especially in cases of serological relapse and sero-resistance, lumbar puncture should be performed to exclude asymptomatic neurosyphilis. Failure of any treatment is always a sign for the use of methods more vigorous than those previously employed.

Re treatment should be on the plan of combined treatment

suggested above for sero-positive primary and secondary syphilis, but with penicillin in heavier dosage. If possible the patient should be hospitalized at the start and given 6,000,000 units in 100 doses of 60 000 units 3-hourly over 12½ days. When treatment has to be ambulant 600,000 units in oil wax suspension should be given daily (for preference in two doses of 300 000 units) for ten days. A second course of penicillin in the same dosage should be given when the second phase of arsenical treatment begins at the fifteenth week.

Cases which have relapsed after any form of treatment are to be watched with great care as they are more liable than are fresh cases to relapse again. Follow-up should include lumbar puncture six months after treatment

Repeated failure after the re-treatment suggested here signifies a high degree of treatment resistance (the fault may lie either in the patient or in the invading organism) and in such cases, fortunately very few the old long term methods with arsenic and bismuth must be used Hyperthermy combined with *arsenic bismuth treatment is said to be very* effective for resistant cases.

LATENT SYPHILIS

The diagnosis of latent syphilis is reserved for those patients in whom blood tests are persistently positive in the absence of any other sign of syphilis clinically in the cerebro-spinal fluid, or as shown by radiological examination of the *heart and great vessels.* Cases of latent syphilis are usually discovered when routine blood tests are performed for example, during pregnancy in blood donors, in patients under treatment for other venereal diseases. Before such a diagnosis is made there must have been found repeated positive blood tests, preferably checked in different laboratories, over an observation period of *three months* (to exclude false positive reactions)

Latent syphilis in young adults or in cases where the history suggests that the infection was recently (within five years) acquired can be treated on the lines suggested for secondary syphilis.

In older people and in cases where the date of the original infection cannot be determined the treatment should be on the lines laid down for late syphilis.

LATE SYPHILIS

I have said before that every case of late syphilis deserves individual assessment, and this holds true when penicillin treatment is contemplated. Improvement both in symptoms and in pathological findings have been reported in varying percentages of cases of all types of late syphilis. It is still far too soon to predict the results of treatment with penicillin alone in late syphilis. Combination of penicillin with other methods of treatment (arsenic bismuth, fever) gives results superior to those obtained with penicillin alone. Practitioners are advised to consult with a specialist in venereal diseases before embarking on the treatment of any case of late syphilis

Benign Late Syphilis

Cutaneous lesions heal rapidly under penicillin treatment. Osseous lesions, if they are recent and superficial (periostitis) sometimes resolve rapidly but older lesions are more resistant and are sometimes quite unaffected. Gummata of the testis react quickly to penicillin.

Before contemplating penicillin treatment of any such case, the condition of the cerebrospinal fluid and of the cardiovascular system must be investigated While investigation is proceeding the patient should receive treatment with bismuth and iodides, and some observers prefer to prepare their patients with such treatment for six weeks or more before beginning penicillin, in order to avoid any possibility of therapeutic shock.

If visceral involvement has been excluded penicillin treatment can begin. The multiple injection method with aqueous solution is to be preferred and patients certainly benefit by being hospitalized. The rest is valuable, and they can be better watched for any evidence of shock. Penicillin should be given 3 hourly in doses of 60 000 units for a total of 100 injections, 6 000 000 units If hospitalization is refused ambulant treatment can consist of two injections each of 300 000 units penicillin in oil wax suspension, daily for ten days. Arsenical treatment can be started on the third day of penicillin therapy provided the patient shows no upset. Mapharside 0·06 gm. or Neohalarsine 0·09 gm. is given twice a week. This treatment, with bismuth once weekly continues when the patient leaves hospital and the standard schedule recomm

for late syphilis (see p 273) can then be followed The total length of this schedule may be reduced (but not to less than six months) if there is a satisfactory response to treatment as shown by clinical and pathological improvement. Observation after treatment in all cases of late syphilis should be lifelong

Visceral Syphilis

Therapeutic shock or paradoxical effects are to be feared in the treatment of visceral syphilis. Syphilis of the larynx hepatic and cardiovascular affections should receive preparatory treatment with iodides and bismuth on the lines already laid down (see p 276) before penicillin is contemplated Information about results of treatment of these rarer conditions is scanty My own experience is limited to a few cases of early (fully compensated) syphilitic aortitis and one case of aneurysm of the femoral artery all of which were treated without the slightest ill-effect after suitable preparation for 4–6 weeks.

If it is decided to use penicillin it is advisable to reduce the possibility of shock by beginning treatment, which must be carried out in bed in hospital, with individual doses of 10 000 units penicillin Provided there is no evidence of shock the dose may be raised at the end of 48 hours to 60 000 units, and the injections then continued until a total dose of 6 000,000 units has been administered Consolidatory treatment can then proceed on the lines indicated above for benign late syphilis, with the proviso that arsenicals are best omitted in cases of hepatic involvement.

Neurosyphilis

Although penicillin does not penetrate into the cerebrospinal fluid in demonstrable quantity during treatment by the methods generally used there is no doubt of its efficacy in neurosyphilis. Symptomatic involvement can be very rapid after penicillin treatment of the earlier types of neurosyphilis, meningitic and meningo-vascular but it is less obvious and less frequent in parenchymatous affections. Improvement in abnormal cerebrospinal fluids can nearly always be obtained but this is not always paralleled by improvement in clinical condition. The commonest changes after treatment are a drop in the number of cells and a reduction in the quantity of protein. Improvement in the fluid may continue up to four

months after treatment, and the best results so far have been seen after treatment with two courses of penicillin given with an interval of a few weeks between them.

There is no indication that results are likely to be improved by the use of intrathecal penicillin and indeed this procedure may be dangerous unless penicillin of the highest degree of purity is used. Therapeutic shock has been reported during the treatment of cases of neurosyphilis, and phenomena so produced have included convulsions and transverse myelitis. Caution is advised, therefore, and all cases should be prepared by treatment with bismuth and iodides before penicillin is used. Preparation should last only 4–6 weeks in the more acute conditions, 10–12 weeks for the chronic. Individual doses of penicillin should be small in the first 48 hours. Hospitalization and treatment with penicillin in aqueous solution is advisable, but good results are reported by American observers in ambulant patients treated with oil-wax suspensions.

In cases of meningitic, meningo-vascular and asymptomatic neurosyphilis the schedule suggested for benign late syphilis is appropriate, patients receiving combined treatment with penicillin, arsenic (arsenoxide for preference) and bismuth. A second course of penicillin (again 6 000 000 units) is superimposed on the continuing arsenic bismuth treatment about 6–8 weeks after the first, and the consolidatory treatment continues. Progress is checked by examination of the cerebrospinal fluid, tests being made at intervals of six months until two successive normal samples of fluid are obtained. The total length of consolidatory treatment will be governed by the clinical response and by the effects on blood and cerebrospinal fluid, but it should certainly be continued for a year after the fluid returns to normal.

Difficulty in assessing results makes it impossible to make even a tentative schedule for treatment of parenchymatous neurosyphilis at present. There is no reason to withhold penicillin in any case. In tabes dorsalis two courses of penicillin, as suggested above, can be superimposed on the old standard schedule using Tryparsamide and bismuth. There is sometimes an exacerbation of symptoms such as lightning pains before improvement begins, but results are seldom spectacular.

In general paralysis penicillin alone or with Tryparsamide and bismuth can be used for those cases in which fever therapy

is contra indicated by poor condition of the patient. Improvement, symptomatic and in the cerebrospinal fluid, is obtained in some cases. Where the patient is fit enough for fever therapy the two methods can be combined Treatment of consolidation *with arsenicals and bismuth will be given whatever the method* of attack.

CONGENITAL SYPHILIS

Prevention. The use of penicillin in the treatment of syphilis during pregnancy is attended with excellent results in both mother and child. Miscarriage, stillbirth and neonatal *death can be averted and children are born apparently healthy* In cases where syphilis is diagnosed late in pregnancy the prognosis for the child is much better when the rapidly effective penicillin can be used The same schedule as that previously described for early syphilis is normally used In cases where complications of pregnancy contra-indicate the use of arsenicals the dosage of penicillin should be raised to 6 000,000 units (100 injections of 60 000 units 3 hourly)

Early Congenital Syphilis

Excellent results are reported from penicillin treatment of *infants with congenital syphilis. Lesions heal rapidly and* positive *blood* tests revert to negative after 2–3 months The dosage *now* recommended by various authors varies between 100,000 to 400 000 units per kilo body weight (and the latter would be my own choice) *The total* is given in divided doses 3 hourly over 7–8 days. In the first 48 hours, to avoid dangerous Jarisch Herxheimer reactions, individual doses should be *low* (2000 units) but they can be appropriately increased after this time. Arsenic bismuth treatment on the scale suggested on page 280 should also be given for ten weeks Prolonged follow up is essential

Late Congenital Syphilis

Results of penicillin treatment in older children are equivocal and seldom spectacular Cutaneous lesions respond well, osseous lesions vary *in response according to their duration.* Interstitial keratitis has, in my experience, responded no better to penicillin than to other remedies, but others have reported dramatic improvement in some cases. Penicillin

should be used in these cases in the manner suggested for late acquired syphilis, with appropriate scaling of dosage of arsenicals used concurrently (p 281)

REACTIONS TO TREATMENT

At least 50 per cent of patients treated with multiple injections of aqueous solutions of penicillin for early syphilis exhibit, in the first day and usually about twelve hours after the first injection, a Jarisch Herxheimer reaction There is fever as high as 104 F which lasts for 12–24 hours and often a transitory oedema around the chancre or exacerbation of a secondary eruption Treatment must not be stopped on this account.

Febrile reactions of this type have been less frequent in patients treated with penicillin in oil wax suspension in larger individual doses, and I have not seen the phenomenon at all in cases of late syphilis

Therapeutic shock is a possibility in cases of late visceral syphilis, but the risk can be *minimized*, as already described, by previous preparation and the use of small individual doses in the early hours of penicillin treatment

Local pain, sometimes severe may occur with certain batches of penicillin in aqueous solution or in oil wax suspension. Variation of sites of injection, massage and heat are all helpful, but it is occasionally necessary to change to a fresh batch of penicillin This difficulty is becoming less frequent as the purity of commercial penicillin increases.

Cutaneous eruptions, due perhaps to impurities in penicillin are sometimes encountered appearing usually four or more days after the start of treatment. Rashes may be localized (buttocks, bathing-drawer area, shoulders) or generalized, and morbilliform, scarlatiniform and urticarial rashes are seen Only in the presence of giant urticaria need treatment cease for fear of oedema of the glottis, and it can begin again with another batch of penicillin when symptoms have subsided. Cutaneous eruptions are treated with Benadryl (an anti-histamine substance) in doses of one capsule (50 mgm.) four times daily

Care should be taken not to mistake such minor phenomena for the more important toxico-dermal reactions (ninth-day erythema) due to arsenicals which may be given concurrently

Chapter XXI

PROGNOSIS OF SYPHILIS

It is possible for a person to escape infection in spite of even repeated unprotected exposures with a known contagious source. When the infection is more than five years old, whether treated or untreated the possibility of spread is slight and continues to decrease as time goes on

The infection is usually spread through contact with early or relapse muco-cutaneous lesions, but seminal infection is possible in the case of patients with early latent syphilis

Infectious relapse occurs in 95 per cent of cases by the end of the third year and is commoner in primary than in secondary syphilis This paradox may be due to a better immunological reaction in the secondary stage. Relapse during treatment usually develops in a period when no arsenical is being given and is commoner in treatment schemes which allow complete lapses from both arsenic and bismuth

Infectiousness bears no relation whatever to the result of the blood test Under continuous treatment patients can be considered to become completely non-infectious after six months.

CURE OF SYPHILIS

The criteria of cure differ from the physician's and from the patient's point of view The possibility of a symptomatic cure, in that the patient will remain completely free of symptoms, is high in all stages of syphilis provided treatment is adequate

The chances of a serological cure are less, but this need not worry the patient The work of Warthin on post-mortem material suggests that biological cure with complete healing and restoration of tissue is impossible but his findings are open to criticism

The fate of the untreated syphilitic is fairly accurately known thanks to the work of Bruusgaard in following up cases who had been under the care of Boeck in Oslo between 1891 and 1910

Boeck believed that the patient's own defence mechanism

was as good as mercury and iodides and accordingly early syphilis was practically untreated Bruusgaard, between 1925 and 1927 followed up 309 patients from the original 2181 and determined the cause of death in 164 others

His findings can be summarized thus if syphilis is un treated 22 per cent of cases will develop fatal or incapacitating late lesions 12 per cent will develop benign late syphilis and 66 per cent will go through life apparently normal Some of this last group will be sero-positive, but the number decreases with time.

Inadequate treatment in early syphilis appears to give results worse than no treatment at all. Neurosyphilis is commoner and its incubation period is decreased. Muco-cutaneous relapse is also likelier The definition of inadequate treat ment can be given as any case in which less than twenty injections of a trivalent arsenical have been given Erratic treatment is just as bad as inadequate treatment.

With adequate treatment the percentage of cures (clinical and pathological) in sero-negative primary syphilis approaches 100 per cent, and in early syphilis generally is more than 90 per cent of symptomatic cures.

Latent and benign late syphilis should have a favourable outcome, as far as the patient is concerned in 80 to 95 per cent of cases. Early neurosyphilis and cardiovascular syphilis yield to treatment in from 70 to 90 per cent of cases Only in parenchymatous neurosyphilis and advanced aortitis or aneurysm is prognosis bad, and even here improvement at least can be expected in most cases.

Early congenital syphilis carries a high mortality rate, but adequate treatment gives gratifying results. The greatest danger in late congenital syphilis is interstitial keratitis, but even here a prompt attack can be effective in arresting progress.

SUMMARY

From the foregoing observations it can be gathered that the early syphilitic can be promised a cure provided that treatment is regular and adequate and that observation is prolonged and complete The definition of cure does not concern the patient.

In cases of symptomatic but not serological cure, observa

tion should be longer and visits more frequent. The tendency should always be to over treat rather than to under-treat — in the sense of time, not individual doses where arsenic is concerned

Proper control after treatment ceases will reveal early neurosyphilis and cardiovascular syphilis in time for effective treatment.

Congenital syphilis should be treated prophylactically so far as possible by finding the syphilitics in antenatal practice. The use of penicillin in treatment, even when pregnancy is far advanced has greatly improved the prognosis as regards the foetus.

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PART III

OTHER VENEREAL AND ALLIED DISEASES

Chapter XXII

RARER VENEREAL DISEASES

CHANCROID (ULCUS MOLLE—SOFT CHANCRE)

This is a venereal disease caused by an infection with Ducrey's bacillus. The incubation period is short, generally from one to eight days Cases are seen oftener in men than in women. True chancroid is not very common in Great Britain and is likeliest to be encountered in cities seaports in particular Chancroid is a purely local infection with no systemic effects immediate or delayed. The disease is almost always confined to the genital area extra-genital infection being very rare.

In the male, the region of the prepuce and frenum is mostly involved in the female, the labia majora or minora. The initial lesion is a craggy ulcer with ragged edges a sloughing base and a red areola, the whole giving an impression of acute inflammation such as is rarely seen with a syphilitic chancre. There is tenderness often extreme tenderness, when the ulcer is being examined. Ulcers may vary in size from a pin's head to about an inch in diameter A solitary ulcer is not common there are usually several sometimes many Once the disease has started spread can occur by auto-infection. A very common type of case shows phimosis with many crack like ulcers at the free edge of the prepuce In some cases hypertrophic lesions are seen in which the ulcerated area becomes elevated as a friable mass of granulations. This type is common in the Mediterranean area.

Lymphatic spread of infection is the rule The inguinal glands on one or both sides are usually enlarged and tender and abscess formation (bubo) occurs quite frequently although not so often now as in pre-sulphonamide days. Chancroidal bubonuli, or little abscesses, along the course of the dorsal

penile lymphatic vessels are occasionally seen A great spread of ulceration starting from an open bubo, is a rare complication known as ulcus molle serpiginosum Gangrene, or phagedena, may rarely occur in conjunction with chancroid

Diagnosis

Ducrey's bacillus is a short Gram-negative bacillus staining more deeply at its ends The bacilli tend to lie in chains It is sometimes possible to find Ducrey's bacillus in smears of material taken from deep in the edge of an ulcer

In actual practice, a diagnosis is made by excluding syphilis, by observing the effects of treatment, and from the appearance of the lesions Any sore on the penis is suspect of being syphilis until proved otherwise. Illustrations of cases of chancroid have been omitted as a deterrent to slipshod clinical diagnosis. Repeated dark-ground examinations are made of serum taken from the ulcers for at least three days running sulphonamide therapy having started as soon as a *tentative diagnosis of chancroid is made* Sulphonamide therapy does not have any effect on the *Spirochaeta pallida* and does not interfere in any way with dark-ground examinations The blood Wassermann reaction is done at the outset and the test is repeated at intervals over three months.

Other methods besides finding Ducrey's bacillus can be used in diagnosis but are really only of academic interest. Auto-inoculation of the lower abdomen by scarifying the skin and rubbing in material from the genital lesions in a positive case produces erythema in twenty four hours and typical ulceration in two to three days The Ito-Reenstierna reaction consists of the intradermal injection of 0·2 c.c. of a suspension of Ducrey's bacillus Dmelcos vaccine or a suspension of sterilized pus from a chancroidal bubo can be used for this test. A positive reaction is shown after forty-eight hours by a red papule, a half to one centimetre in diameter This test does not become positive until the disease has been present for eight days or more, but remains positive for years after an infection A complement fixation test, using Ducrey's bacillus as an antigen is also possible, but here again a positive result is not likely in the earliest stages when it would be most useful.

Treatment

The sulphonamides have a good specific effect on chancroid. Any case of clinical chancroid should start sulphonamide treatment at once while tests for the exclusion of syphilis proceed. All the sulphonamides are effective in doses of 1 gm. four to six times daily for seven to ten days

Local treatment should consist of hot baths and hot saline soaks. No antiseptics are used while the examination for *Spirochaeta pallida* proceeds If phimosis is present subpreputial syringing with saline solution will probably be necessary The average case responds very quickly to treatment and healing may be complete in seven to ten days. Rarely a phimotic case may need a dorsal slit to make local treatment easier if healing is not satisfactory or if there is evidence of phagedena or gangrene, but usually such cases respond as well as any to sulphonamides. Dusting powder can be used as a local application after three to four days when dark-ground examinations have been discontinued.

Hot fomentations may be necessary if there is much enlargement or tenderness of the inguinal glands but adenitis also dies down quickly and the few cases which go on to fluctuation are best treated by wide incision.

When all lesions are healed the patient will remain under observation and have blood Wassermann reactions done monthly for three months. Evidence of double infection with syphilis may appear days or weeks after a chancroid has healed, and lesions which do not heal rapidly with sulphonamides are immediately suspect

Dmelcos vaccine, which contains 225 million Ducrey's bacilli per cubic centimetre, can be tried in very resistant cases It is given intravenously in doses of 1 c.c. 1½ c.c. 2 c.c. 2½ c.c. 3 c.c. at two- or three-day intervals A high fever is produced and the patient must be confined to bed

Penicillin is ineffective against chancroid

LYMPHOGRANULOMA INGUINALE (L. VENEREUM, CLIMATIC BUBO ESTHIOMÈNE)

This venereal disease is most frequent in the tropics, but may be seen anywhere. It is caused by a virus which probably has many strains. It is a disease of the lymphatic structures,

vessels and glands and the original lesion is a small quickly healing sore on the genitals which generally escapes recognition by the patient.

The local lymph glands are affected in 10–30 days after the infection in most cases but occasionally signs may not be obvious for several months The inguinal glands are affected and signs *may be unilateral or bilateral The glands become swollen and* in the mildest cases may after a time, subside without suppuration Generally however the glands suppurate and discharge through the skin forming ulcers and fistulae (Fig 84)

There are, at this time, signs of a general constitutional disturbance, fever malaise and loss of weight Healing is accompanied by the formation of abundant scar tissue. Affection of the anus and rectum, generally confined to women, is accompanied by pain in the rectum and a discharge of blood and pus from the anus

The course of this manifestation of the disease may be very long and is followed very often by the production of a stricture of the rectum The disease must be differentiated from malignant tumour Hodgkin's disease, tuberculosis and bubo due to soft chancre or syphilis

Frei Test

The specific test for the diagnosis of lymphogranuloma inguinale is provided by the intracutaneous injection of 0 1 c.c of Frei's antigen A positive test is shown by an inflammatory papule at least ¼ inch in diameter sometimes with peripheral erythema and central vesicle appearing within forty-eight hours and persisting for several days More than 95 per cent of positive tests are obtained when enlargement of the inguinal glands has become evident The test remains positive in a number of cases for many years after all signs of active disease have disappeared

Frei's antigen is prepared from material taken from buboes in known cases of lymphogranuloma inguinale.

Syphilis should naturally be excluded by repeated Wassermann reactions over a minimum of three months and if a genital sore is present by repeated dark-ground examinations.

Treatment

The sulphonamides are usually rapidly effective especially in early cases. Sulphathiazole or sulphadiazine may be used



Fig. 84.—Lymphogranuloma Inguinale
Top left, ulceration of vulva and anus. *Top right*, and *Bottom left*, simple glandular enlargement. *Bottom right*, ulceration of groin and thigh

in doses of 6 gm. daily for the first three or four days, followed by 3 gm. daily for another week. If no clinical improvement follows one course, after an interval of 10–14 days, another course of a different drug may be tried.

Frei's antigen given intravenously in doses of 0·2–0·3 c.c. every other day has been reported to be of value. The duration of this treatment will depend upon the response obtained. Other methods which may be employed are the production of fever by the intravenous injection of Dmelcos or T.A.B. vaccine intravenously on several occasions at forty-eight hour intervals. The use of intramuscular injections of antimony compounds, such as Fouadin, has also been tried with some success in resistant cases. Penicillin is of doubtful value.

Local treatment may consist, if necessary, of aspiration or incision and drainage of fluctuating glands. Any surgical intervention should be delayed until the effect of chemotherapy has been tried.

Rectal strictures will require long observation and dilatation.

PEYRONIE'S DISEASE

This disease is characterized by the appearance of areas of hardening in the corpora cavernosa. These may vary in size from a mere seed to an area as big as a plum stone. In the more pronounced cases a mechanical effect may interfere with erection of the penis and cause bending of the organ towards the affected side. A large number of these cases are reported by French observers to have a positive Frei test and to have responded well to treatment by intravenous injection of Frei's antigen

GRANULOMA INGUINALE (G VENEREUM)

Granuloma inguinale is a venereal disease due to infection with Leishmania-like organisms. Skin and mucous membranes are involved, chiefly in the genital region, but lesions may be found on other parts of the body Involvement of lymphatic glands is rare The lesions which appear after an incubation period of from several weeks to several months, come first on the site of infection as one or more small papules or pustules which break down become confluent and form vegetations. The condition spreads by peripheral extension and by auto-infection

In the established cases, large shining warty and vegetating areas of granulation tissue are found about the genitals and may in fact, cover the whole genital area and spread to the abdomen and thighs It has been established that the condition is more than a local one, for Donovan bodies have been discovered in the viscera at necropsy in such cases.

The condition is very indolent, shows little or no tendency to heal without treatment and may persist for months or years. The condition has to be differentiated from ulcus molle serpiginosum and from serpiginous syphilides, lymphogranuloma inguinale and fungus or yeast infections of the skin

A positive diagnosis is made by finding Donovan bodies in Giemsa-stained smears of scrapings taken from deep within a vegetation or in biopsy specimens cut from the edge of a vegetation.

Treatment

The value of the sulphonamides in this condition is still unsettled but they are useful for dealing with secondary

infection. The same is true of penicillin. Treatment in the past has been with antimony salts. Tartar emetic can be given every other day by intravenous injections of a 1 per cent solution starting with 3 c.c. and working up to a maximum of 18 c.c.

A course of 20–30 injections is given There should be a rest of at least two weeks between courses

More complex antimony compounds such as Fouadin are given intramuscularly in doses of 1–3 c c every other day for 20–30 days, if tartar emetic is not well tolerated

If the condition responds to treatment it may take several months before healing is complete. Treatment should continue for about four months after all lesions have healed to avoid the possibility of recurrence.

CHAPTER XXIII

OTHER DISEASES ENCOUNTERED IN VENEREOLOGY

NON-GONOCOCCAL URETHRITIS IN THE MALE

URETHRAL discharge in the male can arise from a variety of causes apart from gonorrhoea. The majority of such cases are venereal in that symptoms follow sexual intercourse and are presumably due to infection at that time. It is with this variety that we are principally concerned

The patient complains of a urethral discharge and sometimes also of frequency of urination and dysuria, but these last two are less frequent than with acute gonorrhoea. The incubation period from exposure to infection to the onset of symptoms is usually longer than in gonorrhoea, 7–14 days being the average, but the limits range from 1 to 28 days The discharge is variable in quantity and quality and it may be only an occasional pinhead of mucus, a thin muco-pus, or sometimes a profuse discharge of pus clinically identical with the condition seen in acute gonorrhoea.

It is naturally impossible to make a diagnosis on clinical grounds, and it is usually wise to withhold treatment with sulphonamides until several urethral pus smears have been examined and culture tests made if possible. If gonorrhoea is so excluded specific treatment may be started. The cause is seldom accurately determined in such cases Usually pathological examinations reveal a variety of organisms — streptococci, staphylococci *B coli* diphtheroid bacilli etc but the pus may occasionally be apparently sterile

Some cases are caused by *Trichomonas vaginalis* infestation, but a definite diagnosis of this condition should be made only after seeing the living organism in urethral secretions on direct or dark ground microscopy Liston and Lees (*British J Ven Dis* 16 1940) claim that 16 per cent of cases of non-gonococcal urethritis are caused by *T vaginalis*, but most other observers are much more conservative in their estimates. Presumptive evidence of *T vaginalis* infestation in the male is sometimes obtained when the condition is discovered in the investigation of the female contact.

Some cases may be caused by virus infection but so far no conclusive evidence has been forthcoming in favour of this theory

Urethral discharge may be produced by traumatic means It may *follow the introduction of foreign bodies into the* urethra (straws, hairs chewing-gum and other assorted articles have been described) or the impaction of a stone. The passage of urethral sounds or catheters can also cause urethritis, usually of a *transitory nature. In rare cases urethritis follows the eating* of such things as asparagus or strawberries. Chemical irritants may also be culpable for example, too strong solutions used in irrigation (usually for prophylaxis) and contraceptive pessaries (these may also cause a dermatitis of the penis and scrotum) In the Services chemical urethritis was occasionally induced, usually for the purpose of going to hospital from or to avoid going to, detention barracks. Match heads had a deservedly high reputation in one unit of my acquaintance, but prophylactic creams and ointments were also very effective if introduced well into the urethra.

Excessive coitus, especially combined with excess of alcohol, can also result in a mucoid urethral discharge which clears up without treatment in a few days. A similar condition, vulgarly known as fiancé's gleet may be seen in men who have been indulging in amorous play with prolonged sexual excitement, without actual orgasm.

The story often told by patients, that urethritis is due to coitus with a woman during or just before or after a menstrual period has probably some basis of truth Alteration of the vaginal flora and increases of possibly infective secretions at this time may have a bearing Non-gonococcal urethritis may follow sodomy

It must never be forgotten that urethritis with discharge may occur with other urinary tract infections such as cystitis, pyelitis, etc A syphilitic chancre within the urethra also causes a mucoid discharge but there is usually collateral evidence of syphilis such as local induration and enlargement of inguinal glands, to assist diagnosis

Complications are much less common than in gonorrhoea, but prostatitis, epididymitis littritis, etc may occur (See also Reiter's Syndrome.) Epididymitis in such cases should arouse suspicion as tuberculosis of the urinary tract sometimes

presents in this way In men in the fifties and over chronic prostatitis is often discovered as a cause of a persistent gleet.

When a diagnosis of non-gonococcal urethritis has been made, the patient, thinking anything better than gonorrhoea, is usually much more pleased than his doctor The disease is, in fact, often of much longer-duration than gonorrhoea and there are some cases where it is obvious that time alone is the curative agent Non-gonococcal urethritis may clear away in a day or two without treatment, or it may last for months in spite of the greatest variety of medications. It may indeed become a hobby with some patients.

An attack confers no immunity and seems indeed to make the sufferer more liable to attacks in future.

Diagnosis

Non-gonococcal urethritis is often suspected on clinical grounds if a history of long incubation period is given and if the discharge is thin and mucoid Smear and if possible culture tests are necessary before the diagnosis is finally established If there is any oedema or redness of the meatus, if there is induration along the urethra or if the inguinal glands are enlarged syphilis should be suspected and dark ground examination made of the urethral secretion and, if necessary of fluid obtained by gland puncture. Dark ground examination also demonstrates *Trichomonas vaginalis* and it is good policy so to examine the urethral discharge in all cases of non-gonococcal urethritis if only to exclude syphilis.

The gonococcal complement fixation test is valuable in the investigation of cases with complications such as epididymitis.

If it is possible to examine the woman suspected of being the source of infection some information may be so obtained.

Complete investigation of the renal tract may be necessary in some cases. The possibility of stricture and of prostatic infection should not be forgotten especially in older men.

Treatment

When signs and symptoms are minimal it is often unnecessary to give more than a simple alkaline diuretic mixture such as the following

℞

Sodium bicarbonate	20 grains
Potassium citrate	30 "
Tincture of hyoscyamus	30 minims
Infusion of Buchu to	½ ounce

Half an ounce four-hourly

This mixture can also be given at first in cases where a series of tests is necessary to establish a diagnosis. For the severer cases a course of a sulphonamide, usually sulphathiazole or sulphadiazine for ambulant patients, is often effective. If irrigation with 1 : 10 000 solution of mercury oxycyanide can be given at the same time, so much the better

Penicillin rarely has any effect on the course of true non gonococcal urethritis. It should never be used in any case where there is the slightest suspicion of intra meatal chancre. Penicillin treatment (dosage as for gonorrhoea) should be delayed until the sulphonamides have been tried. Immediate success with penicillin suggests that the diagnosis may well have been gonorrhoea.

Often treatment with specifics produces only slight or transitory improvement. In these cases irrigation is indicated and the changes can be rung on potassium permanganate, mercury oxycyanide and Protargol. Care must be taken not to continue irrigation for so long that a chemical urethritis is produced. When a stubborn case is encountered, the patient must be reassured and kept from continually inspecting and milking his urethra in a search for discharge.

For the most obstinate cases it may be necessary to try pyretotherapy by T.A.B vaccine or even by hyperthermy

Complications are treated in the same way as their counterparts in gonorrhoea.

Progress in any case is assessed by the disappearance of discharge and by the clearing of the urine Follow up should consist of examinations once a week for two or three weeks after treatment ceases, and a final test, as in gonorrhoea, should be done at the end of three months. If penicillin has been used, an additional blood test for syphilis should be made six months after treatment ceases.

REITER'S SYNDROME

Attention has recently been focused on a curious syndrome in which the most constant features are urethritis, polyarthritis

and conjunctivitis Reiter who first described the condition in 1916, believed that he had discovered the cause in a spirochaete, but this observation has never been confirmed.

The patient often presents himself with what is diagnosed as a non-gonococcal urethritis, other signs developing later Gonorrhoeal rheumatism is often closely simulated and until interest was reawakened in the subject, many cases were doubtless so diagnosed. In a genuine case, however the gonococcus cannot be found in urethral or ocular secretions and the gonococcal complement fixation test and tests for syphilis are negative. Culture tests are frequently sterile

A virus as cause has been suggested by Harkness, who claims to have demonstrated inclusion bodies in discharge.

The same symptom complex has also been described as occurring with or after an attack of bacillary dysentery and bloody diarrhoea was noted by Reiter in his original case.

There is good reason to believe therefore, that this disease *is not or at least not always, venereal in origin*

The patient is usually a young adult male (the oldest seen personally was fifty-five) who presents himself with a purulent or muco-purulent urethral discharge and later develops polyarthritis and conjunctivitis. The urethritis often lasts for only a few days, clearing up with sulphonamides. Large joints are commonly affected and there is pain on movement tenderness periarticular swelling and often considerable synovitis.

Conjunctivitis is bilateral and varies from a slight reddening with photophobia to a severe purulent type Iritis and keratitis have been noted but permanent damage does not occur

In the early stages there may be fever diarrhoea and occasionally generalized erythematous eruptions. Circinate *balanitis and cutaneous lesions of feet and legs indistinguishable* from keratoderma blennorrhagica are sometimes seen I have recently seen a patient who exhibited icterus of the conjunctivae for 48 hours during the first week of the disease

The clinical picture is variable, and although the classical triad of urethritis, conjunctivitis and arthritis is seen in most cases, one or other may be entirely omitted The disease runs a long course, often punctuated by flare ups, and relapse may occur after apparent cure Patients seldom reach the convalescent stage under a month and *it is not unusual for the* disease to last two or three months.

In differential diagnosis there must be considered gonorrhoea (excluded by pathological investigation) acute rheumatism (which responds to salicylates while Reiter's disease does not) and possibly syphilis if penile lesions are present.

Treatment

Conjunctivitis and urethritis usually respond to a course of sulphathiazole or sulphadiazine. Irrigation may be necessary for persistent urethral discharge.

Rest in bed is essential for the arthritis which does not respond to sulphonamides or salicylates. Local heat by kaolin poultices or infra red irradiation is helpful and patients should be encouraged to keep up gentle active movements

Penicillin is quite useless even in doses of 3–4 million units The few cases (none having bowel symptoms) in which I have used sulphaguanidine have not improved any faster than with other methods.

After treatment has ceased it is advisable to have a follow up on the lines indicated for non-gonococcal urethritis.

AFFECTIONS OF THE GLANS AND PREPUCE

Phimosis is a condition of the prepuce in which the orifice is so narrow that its retraction over the glans penis is difficult or impossible even in the absence of disease The preputial orifice may be so small that it interferes with urination, and irritation caused by urine and retained smegma combined with superadded infection produces a superficial inflammation of the glans and inside of the prepuce commonly called balanitis but more properly balano-posthitis Balanitis with phimosis may result in adhesion of the prepuce to the glans Sometimes a retracted phimotic prepuce cannot be pushed forward over the glans, and swelling and oedema of the prepuce cause the condition known as paraphimosis

Phimosis

The patient with irreducible phimosis is liable to attacks of balanitis, and should he contract venereal disease, the condition makes treatment difficult. The treatment of election here is a circumcision done if possible when the organ is not inflamed If, however phimosis is delaying treatment in a case of sore or urethritis, circumcision must be done at *once* or if it is not

possible a dorsal slit of the prepuce should be made and the operation of circumcision completed if necessary when inflammation has subsided (Fig 85)



Fig 85.—Phimosis
In this case syphilitic chancre was concealed

Phimosis with balanitis produces swelling and oedema of the prepuce with a moderate or slight degree of phimosis the swelling produced by balanitis or superadded venereal disease may make the condition irreducible. Before circumcision or a dorsal slit in such cases, the condition is treated locally by frequent hot baths hot soaks in a saturated solution of magnesium sulphate and by subpreputial syringing with the same solution to reduce the inflammation Sulphanilamide 4 gm daily for 4–7 days is also useful if a sulphonamide is not already in use for a gonorrhoea

For the operation of circumcision a local anaesthetic is used in clean cases but if there is gross infection a general anaesthetic must be used

If operation is refused the patient must be instructed to keep his penis as clean as possible by frequent washing with soap and water as a prophylactic measure

Paraphimosis

This condition arises when a tight prepuce is retracted and cannot be drawn forward again It may occur after and is often associated with gonorrhoea or sore on the penis when the inflammation so produced renders the preputial orifice even narrower than normal The orificial ring catches in the coronal sulcus and in a short time the prepuce becomes

oedematous, the chief collections of fluid being between the constricting ring and the corona above, and behind the constriction on the under surface of the penis. These fluid collections soon swell up and look like little bladders (Fig 86) It is astonishing how long the average patient contemplates his swollen organ before he brings it for attention After twenty four hours or so it is common for some ulceration to begin as a crack over the upper surface of the constricting ring, the glans becomes a little swollen and the whole surface is red, moist and irritated



Fig 86 —Paraphimosis
Oedema of retracted prepuce. No venereal disease in this case

If nothing is done the ulceration becomes deeper until eventually the constricting ring is broken, in fact a self produced dorsal slit, and the swelling gradually subsides. Gangrene or major damage due to untreated paraphimosis is surprisingly infrequent

Treatment. If the patient seeks treatment early before gross swelling or ulceration, there is no difficulty in effecting a reduction. Wipe the penis clean and dry and with the patient lying on a couch, hold the penis behind the constriction between the middle and forefingers of both hands and press the two thumbs on the glans Pull the constricting ring upwards as if lifting the patient off the couch by his penis and at the same time use the thumbs to ease the glans down through the ring The vast majority of cases are easily reduced although the manipulation often causes considerable pain Do not use lubricants to try to make reduction easier as they only make the fingers slip Bare hands are best, but gloves should be used if any sores are present.

If this is not successful, apply hot soaks of saturated solution of magnesium sulphate to the penis for an hour or two and try again Nitrous oxide anaesthesia may turn the scale if available.



Fig. 87 —Erosive Balanitis

Should manipulation fail entirely the constricting ring must be cut If there is not too much sepsis a local anaesthetic can be used but if there is ulceration it is best to employ gas and oxygen or an intravenous anaesthetic. Once the ring is cut, hot soaks are continued swelling soon subsides and reduction is easy Circumcision is advised to avoid recurrence, but should be delayed until all swelling has subsided

Balano Posthitis

Infection of the surface epithelium of the glans and prepuce occurs oftenest in phimotic subjects, particularly those who pay the least attention to hygiene. Sometimes balano-posthitis may follow sexual intercourse and can be presumed to be venereal in origin It occurs also with gonorrhoea but is rarely caused by the gonococcus itself In the mildest form the surface of the glans and prepuce is red rough and granular and often there is erosion of the epithelium in patches with actual ulceration in the worst cases There is usually some oedema of the prepuce (Fig 87)

Balano-posthitis is sometimes due to infection with *Trichomonas vaginalis* the parasite being acquired during sexual intercourse with an infected woman

Certain cases of syphilis, particularly in the earliest stages closely simulate balano-posthitis and any patient with ulceration should have dark-ground examinations done for several days It will also be wise to repeat Wassermann reactions monthly for three months in all cases to exclude syphilis

Treatment The penis should be washed and soaked frequently with hot saline solution or magnesium sulphate solution and subpreputial syringing will be necessary if there is an associated phimosis. No antiseptic must be used if dark-ground

examinations are being made. After washing a dusting powder is applied and in the worst cases a sulphonamide by mouth is often effective.

In the mildest cases without gross phimosis the condition is often cured very rapidly by swabbing with methylated spirit and then using a dusting powder One application is usually enough and this is fortunate, for few patients will submit twice to the treatment. The condition usually subsides with local treatment, even the worst being cured within 10–14 days. The patient is advised to keep his penis well washed in future. If there is phimosis or if the attacks are frequent a circumcision should be done A dorsal slit may be necessary in some cases if phimosis makes treatment difficult or if it is suspected that a sore may be concealed

Very rarely a balano-posthitis with phimosis may go on to actual gangrene or phagedena. The prepuce becomes brawny and later a black discoloration appears at the gangrenous area If this is suspected a dorsal slit should be made at once and treatment with penicillin or a sulphonamide begun at once This complication is fortunately uncommon and has become even more so with sulphonamide treatment In the worst cases the gangrene can spread down the shaft of the penis and even to the scrotum and abdominal wall, necessitating wide incisions. Such cases are gravely ill.

CONDYLOMATA ACUMINATA

Warts are common on or about the genitals quite apart from venereal disease, and it is very unwise to accuse a patient of having venereal disease on this evidence alone In men warts occur with greatest frequency on the glans and prepuce round the anus, on the shaft of the penis and within the meatus in that order (Fig 88) Some degree of phimosis is common and warts are rare in the circumcised In women warts occur mainly on the labia and may extend back to the anus (Fig 89) Moisture seems to be an important factor hence the distribution.

It is not uncommon to find a growth of warts with or after gonorrhoea in both sexes. The condition may vary from a solitary small wart to a state where the whole glans and under surface of the prepuce or the entire surface of the

Fig 88.—Condylomata Acuminata
Left, warts at preputial orifice ; *Right*, the same case prepuce retracted

labia majora is solid with growth and looks like a cauliflower

Diagnosis

Common warts in the genital area must be distinguished from the condylomata lata of secondary syphilis The latter



Fig 89.—Condyloma Acuminata on the Vulv

are moist, reddish brown or purplish papules found in the same situations, but they are never sessile or pedunculated as is usual with common warts. There will usually be some other evidence of syphilis, and the Wassermann reaction is invariably positive if the disease has progressed as far as the formation of condylomata lata. All cases of warts should be investigated with regard to gonorrhoea, and if any active disease is discovered it must be eradicated or the warts will probably recur after treatment.

However if there is no history of gonorrhoea and if there is no discharge and the urine is clear the investigation in the male need not be very complicated

Treatment

By far the best treatment in all cases is a complete removal of the warts with the electrocautery A few solitary small warts can be burnt off without an anaesthetic, but it makes the operation much easier if the bases are injected with 2 per cent novocaine. When the condition is more widespread an anaesthetic is essential. Two per cent novocaine with adrenalin can be injected under the affected area, but if in the male the whole glans and prepuce are affected it is best to do a block anaesthetic by making a ring of novocaine round the penis, half-way down the shaft. For local anaesthesia the use of a dental syringe and needle is strongly recommended as the process of injection is then almost painless.

Bleeding is apt to blur the field when warts are numerous and is least with local anaesthesia but sometimes a general anaesthetic may be considered necessary

The warts should, if possible, be picked up with forceps and cut off at the base with the cautery but when a large area is covered, they can be scraped off with a spoon or scalpel and the area cauterized. It is best to do the whole job at once and touch up any stray pieces later when the consequent inflammation has subsided After cautery hot saline soaks are given and the area is dusted with talcum powder If there is a co-existent phimosis recurrence is much less likely if a circumcision is done and all remaining warts cauterized

If no electrocautery is available caustics have to be used, and the best results are obtained with a suspension of podo-

phyllum resin (25 per cent) in water liquid paraffin or acetone The *area to be treated must be ringed with Vaseline* Results are quite good if there are only a few warts, but treatment may have to be repeated after an interval of a week. Fuming nitric acid or trichloracetic acid can also be used It is good policy to have a Wassermann reaction done in all patients with warts whether venereal disease is suspected or not

SCABIES

The itch is caused by infection with the parasite *Sarcoptes scabiei*. The disease is in many cases venereal that is to say it is contracted by close contact with an infected person during sexual intercourse. In such cases the original lesions are often *in the genital region and in men lesions on the penis may be* confused with early syphilis. Moreover it is possible to have a double infection of scabies and syphilis a chancre developing on top of a scabies lesion Scabies is the commonest of skin diseases and also paradoxically the one least often recognized by the general practitioner

The main symptom is itching worst at night or when the patient is warm *Any skin disease in which itching is prominent* should be suspected of scabies until proof is available that it is something else The lesions of scabies are found mainly in the following situations (1) the webs of the fingers, (2) the fronts of the wrists (3) the backs of elbows, (4) the anterior folds of the axillae, (5) round the waist (6) on the male genitalia (7) on the buttocks, (8) on the ankles

On the hands and wrists the burrow or run produced by the tunnelling of the female (Fig 90) mite can often be seen as a line under the epidermis, white in clean people black from dirt in other cases. Elsewhere on the body burrows are not so common the lesions being red papules often scratched and sometimes scabbed if there is a superadded impetigo On the penis and scrotum the lesions are hard red lumps often as big as a split pea, usually with a small crust on top A solitary genital papule is sometimes seen but there are usually others to be found locally or elsewhere on the body Inguinal adenitis may be found but the glands have not the feel of those present in syphilis. Ulceration of scabetic papules on the genitals does occur but to the skilled eye the appearance is

seldom likely to lead to a suspicion of syphilis. Repeated dark-ground examinations, and Wassermann reactions over three months will exclude the possibility of syphilis in doubtful cases.

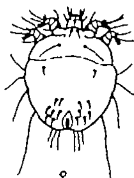


FIG 90.—SARCOPTES SCABIEI

Treatment

Sulphur The patient takes a long hot bath, rubs himself all over with soft soap and scrubs himself or better is scrubbed with a nail-brush to open all burrows He then dries himself and rubs in sulphur ointment all over the body from neck to toes with special attention to the sites of election of the parasite Treatment is best done at night so that the patient can go at once to bed The treatment is repeated on three successive nights, and on the fourth morning a fresh and complete change of clothing is worn after a bath and all clothing and bedding previously used is sent off for disinfestation It is a good plan for the patient to wear at night and during the treatment a thin suit of pyjamas so that the ointment is kept in close contact with the skin all the time and the clothing is protected.

Benzyl benzoate One or other of the following lotions may be used (1) equal parts of benzyl benzoate and methylated spirits (2) benzyl benzoate 25 per cent, Lanette wax 2 per cent, water 73 per cent The patient is bathed and scrubbed as before, dried and then painted all over with the lotion, which is allowed to dry Another painting is then done at once. The patient does not wash for twenty-four hours and then has another similar treatment Twelve hours later after a bath fresh clothes are worn and the old clothes and bedding are disinfested

The necessity for disinfestation of the clothing and bedding after treatment has recently been questioned but if it is possible to have it done it is a wise precaution.

PEDICULOSIS PUBIS (CRABS)

Infestation by the crab louse (*Pediculus pubis*) is usually contracted by adults during sexual intercourse, but may be acquired from lavatory seats and other sources.

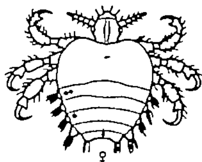


Fig. 9 —Pediculus Pubis

The hair of the pubis, lower abdomen and anal region is commonly affected but the parasite may migrate as far as the arm pits, eyebrows and eyelashes, and in hairy individuals widespread distribution can occur (Fig 91)

The only symptom is itching and this varies from the slightest discomfort to intolerable irritation

The lice are about the size of a pinhead and may be grey brown or red in colour They can be seen moving on skin or hairs. Nits are fixed to the shaft of the hairs above the surface of the skin.

Maculae ceruleae, bluish-grey macules are sometimes seen with *Pediculosis pubis* and are caused by the injection of a secretion when the parasite feeds.

Treatment

The quickest and easiest cure is to shave the affected parts and apply 2 per cent ammoniated mercury ointment There is no need to disinfest clothing If the eyelashes are infected the nits and parasites are picked off with forceps and golden ointment applied

TRICHOMONAS VAGINALIS INFESTATION

Trichomonas vaginalis is a distinct species of a series of flagellate protozoa parasitic in man Infestation of the genito-urinary tract causes symptoms in both men and women and the mode of passage is sometimes venereal It has been suggested that *T vaginalis* may be found in the normal vagina, but that it produces symptoms only after trauma. Other parasitic trichomonads are found in the human species in the mouth and intestine.

T vaginalis is pyriform in shape and has four anterior free flagellae, a fifth along the edge of an undulating membrane and a posterior axostyle. In size and shape it resembles an epithelial cell, and when immobile, as in stained specimens,

is difficult to distinguish from epithelium (Fig 92)

The diagnosis of *T vaginalis* infestation is made by finding the protozoa in suspect discharges by examination of wet specimens in a hanging drop by direct illumination or by dark ground examination of a wet film. A thick discharge may be diluted with normal saline solution before examination The living and moving parasites may be seen by this method. In making direct examinations the secretion may also be diluted with a drop of 0 1 per cent safranin solution, which stains pus cells pink but leaves the protozoa unstained and unaffected in motility The thrashing flagellae and movement of the protozoa make recognition easy

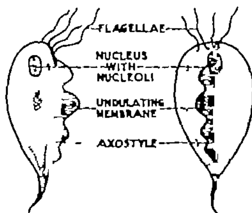


Fig 92.—TRICHOMONAS VAGINALIS

Culture tests and examination of Leishman-stained specimens are also used in diagnosis, but the wet specimen technique is best for general purposes and stained specimens are difficult of interpretation for the unskilled eye.

A In the Female

T vaginalis infestation can produce a vaginitis in women acute or chronic in character Other infections such as gonorrhoea may coincide with *T vaginalis* and the diagnosis of a gonorrhoea may be made more difficult if the two are present Discharge persisting after a fully treated gonorrhoea is quite often due to a *T vaginalis* infestation Acute infection is characterized by a profuse frothy vaginal discharge. The vaginal wall is inflamed and often studded with red spots deeper in colour than the general background.

In chronic vaginitis the discharge may be thin and serous and clinically the condition is indistinguishable from any other leucorrhoea. *T vaginalis* infestation is very common and up to 25 per cent of cases in any venereal disease clinic may be

found to harbour the parasite with or without clinical signs.

The diagnosis is made by finding the protozoa in the vaginal secretion

Treatment Acetarsol, a pentavalent arsenical has a specific curative effect This drug is known commercially as Stovarsol or Acetarsone, and is applied locally to the vagina as a powder or in a vaginal tablet. The powder can be blown into the vagina with an insufflator or dusted in through a speculum. The patient should attend daily or every other day for treatment

The vagina is cleaned by swabbing or douching with sodium bicarbonate solution and the powder applied Preliminary painting with 1 per cent gentian violet solution is sometimes advocated. Treatment should continue through the first menstrual period and for two weeks afterwards Symptoms abate rapidly but relapse is fairly common usually occurring after a menstrual period and it is wise to give treatment for a week after two subsequent periods If the patient is unable to attend for treatment, she may insert two to four acetarsol tablets high into the vagina daily at first and later every other day when the discharge has diminished

Carbarsone another pentavalent arsenical gives better results when the patient is treating herself This drug can be obtained in the form of soluble vaginal suppositories (Eli Lilly & Co) and is better distributed over the vaginal surface than are acetarsol tablets Arsenical toxic effects are very rare and acetarsol or Carbarsone can safely be used during pregnancy or at any time

Silver picrate and Negatol by local application and in pessary form can also be used but offer no advantages over the methods described

B **In the Male**

Infestation in the male may vary in extent from the preputial sac or urethra to the whole genito-urinary tract Prostatitis and epididymitis suspected of being due to *T vaginalis* have been described Frequently a trichomonas urethritis is of a mild and transitory nature, but sometimes gonorrhoea is simulated

Male infestation is usually contracted in sexual intercourse, and in marital cases particularly it is important to examine the female contact and institute treatment.

Diagnosis is made by finding the protozoa in urethral discharge.

Treatment The majority of cases of urethritis will be cured by making the urine strongly alkaline. Irrigation is unnecessary and may be harmful. Relapse after coitus or alcohol may be due to persistence of the organism in the prostate gland.

ULCUS VULVAE ACUTUM

This is a disease of young women Though it is in no sense a venereal disease, occurring as it may in virgins, its recognition is important in differential diagnosis

The vulva is sore and extremely tender to touch and there is often fever at first On the labia, particularly the labia minora, are many deep soft ulcers, irregular in shape, and with red areolae. The ulcers range in size from a pin point to an inch in diameter In the worst cases there can be necrosis and gangrene with perforation of the labia minora

The Gram-positive Bacillus crassus can always be found in the secretions The disease runs its course in ten to fourteen days but relapse is common. Chancroid and syphilis have to be considered in differential diagnosis, and the investigations will always include a blood test for syphilis

Treatment. The patient will require complete rest in bed Local treatment consists of frequent potassium permanganate baths followed by application of a simple dusting powder

PART IV

TECHNIQUE

Chapter XXIV

PRACTICAL INSTRUCTIONS

IRRIGATION

Until the advent of the sulphonamides, the most important method used in the treatment of gonorrhoea in the male was urethral irrigation This form of treatment was introduced about the beginning of this century and was popularized by Dr Jules Janet whose name is often associated with the procedure. Previously local medication of the urethra had been done by instillation of solutions by means of a syringe. The results of irrigation or lavage treatment were very good when all treatments were performed by a person skilled in the technique and were quite satisfactory in clinic practice where, after a few days patients had to be left to fend for themselves.

Irrigation has often been blamed for producing complications such as prostatitis or epididymitis but this has been much exaggerated and in cases where individual attention is given complications were, and are, very rare. When the patient has reported early the beneficial results of irrigation are due to the mechanical washing effect and to a lesser extent to the direct action of the antiseptic solution used

Irrigation is classified into two types anterior irrigation when the urethra is washed only as far as the external sphincter of the bladder and posterior or bladder irrigation where the solution is allowed to fill the bladder and then be passed out again by the patient.

The combined use of irrigation and sulphonamide therapy gives the best results in all types of cases and irrigation alone has an important place in the treatment of primary and secondary non-gonococcal infections of the urethra The apparatus is simple a good technique can quickly be

mastered, and no harm can be done by the tyro provided he does things gently until he has gained confidence.

Apparatus

The requirements are a glass container to hold at least two pints a length of rubber tubing with an easily operated clip to control flow through the tube, a urethral nozzle, and a receptacle to catch the used fluid

The container should be on an adjustable stand so that it can be raised or lowered or hooks can be put at different heights on the wall to hold it. A glass container is best as the run of the fluid can be seen an important point in posterior irrigation The rubber tubing should be of sufficient length to stretch easily from the patient to the container in any position.

The best clip for the tube is one large enough to be operated by the whole hand for it is very fatiguing and clumsy to have to use the small clips which are opened by pressure between finger and thumb

Irrigation can be done with the patient standing up or sitting upon a couch. The latter position is better as it provides easiest access and control. A receiver between the thighs collects the irrigating fluid as it escapes from the penis. A small basin can be used, but if it is intended to treat any number of cases, it is wise to provide something better The best container is a somewhat oval basin shaped to fit the triangular space between the thighs and deep enough to rest on the couch (Fig 93) The sides are carried out as wings to fit over the thighs and the narrow end has a depression cut from it so that the penis and scrotum hang comfortably into the basin Such containers are not in common use but any tinsmith will make one from zinc or tin plate to order for a very small sum

A paper towel is laid over the patient s abdomen to protect him from splashes and for use afterwards for drying For ordinary purposes the simple Janet nozzle of glass or metal is very satisfactory The container and tubing should be sterilized by boiling every morning if possible and at least twice weekly Nozzles are kept in the sterilizer

The Irrigating Fluid

The solutions which should be kept ready are potassium permanganate, oxycyanide of mercury and acriflavine. Con

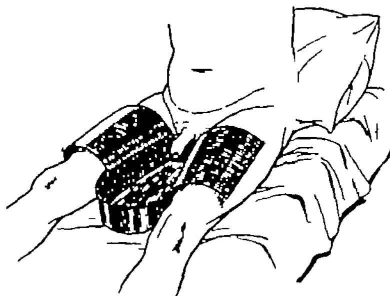


Fig 95.—Receiver in Position for Irrigation

centrated stock solutions are made up The irrigating fluid is usually one part of the drug in ten thousand of water A concentrate containing 28 grains in 92 oz., a 1 500 solution is a useful strength 1 oz. in a pint of water giving a 1 10 000 solution The temperature should be within a degree or two of 108° F

Other solutions such as silver nitrate Protargol zinc permanganate, methylene blue, etc can be used for irrigation but for the vast majority of cases the three mentioned above will be ample

Technique

The patient sits on the examination couch with trousers off and the receiver is placed in position He has previously been examined and has urinated A sterilized nozzle is put on the end of the tubing 2 pints of warm water poured into the container and 2 oz of the stock solution to be used is added The clip is opened and lotion run through to drive the air from tube and nozzle.

Anterior Irrigation

The container is set with the upper level of the fluid at a height of 2–3 ft above the level of the patient s pelvis For

the first irrigation for any patient, 2 ft of pressure is high enough. Once the patient is used to the sensation 3 ft of pressure is better The operator stands at the patient's right side and holds the patient's penis in his left hand with prepuce retracted The right hand manipulates the clip and regulates the flow of fluid The clip is placed as close to the nozzle as possible so that the right hand can also direct the nozzle.

The glans is washed with a jet of fluid which is then directed at the meatus, the lips of which are held apart Next the nozzle is put into the meatus and fluid is allowed gently to flow into the urethra. If the finger tips of the left hand are rested on the under surface of the urethra, the fluid can be felt gradually to dilate the canal, which becomes tense.

The flow of fluid is then stopped The nozzle is pulled back a little and the urethra is allowed to discharge its contents into the receiver When the urethra is emptied the nozzle is pushed forward again and the procedure repeated This is done again and again until the lotion is exhausted. With practice a two-pint irrigation can be done in about five minutes No pain should be felt by the patient and the nozzle should be removed at once if he complains Naturally the sensation is a little odd the first time irrigation is done but the patient must be told that he should endure this and give warning only of actual pain

Posterior Irrigation

This is always preceded by an anterior irrigation with the first half pint of fluid Even before the patient is instructed in the procedure, a little fluid finds its way into the bladder during anterior irrigation but for a real bladder wash some preliminary instruction is necessary

The patient is told to relax completely and try to simulate that state attained in urination after the act has started, when th urine flows of its own volition without pressure. To do this he may have to try to urinate against the fluid and then relax. Some patients find it best to retain a little urine in the bladder

The upper fluid level must be 3 ft. above the patient and in some difficult cases, 4 ft. of pressure is necessary

After the anterior irrigation has been done, the nozzle is held fast in the urethra. The fluid is run in, the clip being

kept open and the patient told to relax. After a few times the patient will find that he can allow the fluid to run back into his bladder At first only a few drops may pass before the sphincter rebels, but soon it will be possible to fill the bladder When this is done, the fluid is urinated back into the receiver and the proceedings are repeated until the fluid is used up

Posterior irrigation is much easier to initiate with a sitting than with a standing patient *Brute force by high pressure* must never be employed to give a posterior irrigation. It is rare that a patient cannot learn the technique if the medical attendant has the time and patience to devote to him.

There are many ways of helping the difficult case to start such as telling him to keep a little urine in the bladder so that he can attempt to relax his sphincter by urinating against the pressure, lying back and closing the eyes, and oddly enough pulling the pubic hair

In treating acute cases, particularly out patients irrigations should be done twice daily morning and evening for the first week. As soon as possible after the first two days, posterior irrigation begins Gentle irrigation is of the greatest value in all cases with urethral discharge. In the presence of acute complications such as prostatitis or epididymitis the beginner will be advised to suspend irrigation treatment until resolution begins, but a skilled operator may continue anterior irrigation throughout.

ANTERIOR URETHROSCOPY

The urethroscope is a luxury in general practice. Nearly all the information urethroscopy can yield is discoverable by the proper assessment of clinical findings and by the use of straight or curved metal sounds The varying appearances of the normal and abnormal urethrae can be learnt by constant practice such as is possible only in a venereal diseases clinic.

If the practitioner having spent some time in a clinic, decides to acquire an instrument his best choice is the Harrison anterior urethroscope with three tubes sizes 20 22 and 24 Only an anterior urethroscope need be obtained for posterior urethroscopy is a difficult and often unsatisfactory proceeding

Anterior urethroscopy is absolutely contra indicated in the

presence of acute urethritis In uncomplicated gonorrhoea or non-gonococcal urethritis urethroscopic examination can be made at the end of the active treatment phase, when the discharge has ceased and the urine is clear and again at the test of cure. In subacute or chronic urethritis urethroscopy may disclose evidence of littritis, of submucous infiltration or of polypi. The face of a stricture can sometimes be seen with the urethroscope and the appearances may help in choosing instruments for its dilatation. Cautery and other operative procedures which can be done via the urethroscope are best left to the specialist.

Description

The Harrison urethroscope consists of a hollow tube with an obturator fitting inside. The tube has a smaller side bore along which can be passed the rod carrying the illuminating bulb The optical system is attached to this rod and the whole fits closely into the top of the hollow urethroscope tube At the sides of the optical attachment are a tap to which a rubber bellows can be fitted, and a pin to which the wiring goes Current for the bulb can be obtained from a dry or wet battery a pantostat or a transformer A rheostat is necessary for control.

For the purpose of sterilising the tube and obturator are boiled, but the rod and lamp are wiped with spirit and left in a formalin cabinet.

Directions for Use

For inspection purposes the patient should not urinate before the operation He lies on his back on a couch and the glans is cleaned with spirit. All the rules of asepsis are followed A sterile tube of suitable size, with obturator in position is lubricated with sterile liquid paraffin and passed down the urethra until the flange rests on the glans No force is necessary The obturator is withdrawn and a sterile cotton-wool dressed probe is passed down to mop up moisture and excess lubricant.

The light is switched on and the bulb on its rod is passed down the side tube until the optical attachment fits firmly on the tube The bellows is in position and inspection can begin. By gentle inflation the urethral wall is stretched and all its surface brought into view (Fig 94)

Slowly withdrawing the tube and squeezing the bellow



Fig 94.—URETHROSCOPY
Left, drying the tube *Right*, optical apparatus and bellows in position for viewing

from time to time, the whole of the anterior urethra to the tip of the penis can be seen

After the operation the patient should be irrigated with a 1 10 000 solution of mercury oxycyanide If bleeding occurs it is best not to proceed with the examination because air embolism is possible, though very rare, when the urethra is inflated No special measures are necessary to control any bleeding which will quickly stop of its own accord.

The normal urethra is smooth and pink or red in colour and blood vessels can be seen in its walls Under air pressure it dilates quickly to smooth out the rugosities and the underlying musculature can give an appearance almost of rifling Openings of glands and lacunae can be seen

In the abnormal urethra strictures and fibrous patches are easily seen. Pus may exude from ducts of infected glands. Infiltration of the mucosa is shown in injection of the wall and diminution or absence of the normal dilation on pressing the bellows.

DARK-GROUND EXAMINATION

Collection of Specimens for Immediate Examination

Material for examination for *Spirochaeta pallida* can be obtained from genital or extragenital sores from secondary syphilitic lesions such as condylomata lata, mucous patches, skin papules and from the enlarged inguinal glands associated with primary sores

S pallida is most easily found in serum from primary sores or from moist secondary lesions such as condylomata lata The lesion chosen is cleaned with a swab of gauze or lint soaked in saline and the surface is rubbed This will in the case of primary sores or condylomata lata, produce some bleeding or oozing of serum but the lesion may have to be squeezed between finger and thumb Dry lesions will have to be scraped with the edge of a scalpel first. Blood-stained specimens are not good material for examination, and the lesion must be mopped until a clear serum oozes Healed or healing chancres must be well scraped and squeezed to make serum from the depths of the sore exude, because the surface serum is often sterile in such cases. Here the use of a tourniquet on the base of the penis for five minutes after scraping may help to produce a suitable specimen

When a bead of clear serum has collected it is picked off by touching it gently with a cover-slip held between the fingers or in a cornet forceps Serum from the edge of a primary sore is likeliest to contain the organism. The cover-slip is placed on a thin clean and unscratched microscope slide so that the serum spreads out between slide and slip The slide is put face-down on a piece of blotting paper and pressed firmly on to the cover-slip so that the serum is spread thinly between them.

To obtain a specimen from an inguinal gland a hypodermic needle on a tight syringe is pushed through the skin and into the gland A drop or two of sterile normal saline solution is injected the gland is rolled between finger and thumb for a few moments, and a fluid mixed saline and gland serum, is sucked back into the syringe. A drop of this fluid is expressed on to a cover-slip and a specimen prepared for examination as described above.

Collection of Specimens by Capillary Tube

This method is used when the specimen of serum has to be sent away to a laboratory for examination but is also very useful in collecting serum from inaccessible places such as mouth lesions or sores on the female genitals particularly on the cervix.

A fine glass capillary tube about five inches long is suitable for most purposes and can easily be prepared by drawing out glass tubing in a flame. The lesion is cleaned and prepared in the manner already described One end of the tube is dabbed along the edge of the lesion and capillary action causes serum to flow up into the bore. A quarter to half an inch of serum is easily obtained.

If the serum is to be examined at once, the empty end of the tube is put in a flame which seals it, and expansion of air between the serum and the sealed end expresses the serum which is collected on a cover-slip and prepared for examination

When the tube is to be sent away for examination the empty end is heated over a flame for a moment and then sealed completely by holding it in the flame. The preliminary heating causes expansion of air in the tube, and when the end is sealed and the air cools and contracts in volume, the serum is drawn a little way up the tube, leaving an empty space. The end of the tube nearest the serum can now be sealed in the flame, but this is really unnecessary and there is a danger of overheating the serum in the process. *S pallida* remains alive in capillary tubes for many weeks

Preparation of the Microscope

It is essential to have this demonstrated in the first instance but the main principles can be recapitulated The basis of dark-ground microscopy is that the images seen are produced by reflected and not by transmitted light (Fig 95) The illumination is so directed by the special condenser that a conical beam of light reaches its focus in the serum to be examined and then passes on so that none goes directly through the objective lens to the eye. Light striking solid material in the serum is reflected by it and some rays pass through the aperture and are appreciated by the eye

A. Source of Light A strong light is necessary and a Pointo-

light lamp or carbon arc with a bull s-eye to concentrate the beam on the reflecting mirror is recommended The beam is reflected by the plane mirror on the microscope so that the maximum illumination is central on the top surface of the condenser Some types of apparatus can be obtained in which the source of illumination and the dark-ground condenser are incorporated in one piece

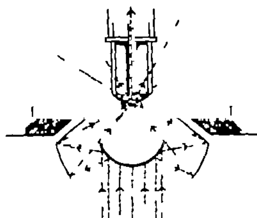


Fig 95.—Optical Principle of Dark-ground Microscopy

B The Dark Ground Condenser This must be quite centrally placed under the objective. For this purpose a series of concentric circles are etched on the upper surface as a guide Centring is done by focusing through the 2/3" objective on the upper surface of the condenser when the rings become visible They are brought into the centre of the field by manipulation of two screws at the sides of the condenser frame (Figs. 96 and 97) In some cases the rings are more easily seen if a drop of oil is put on top of the condenser



Fig 96.—Microscope with Dark-ground Condenser to show Centring Screws

C Placing of the Slide A spot of oil—paraffin or cedarwood—is put on the cover slip on the under-surface of the slide, and on the condenser top The condenser is racked down and the slide put in position on the movable stage. When the condenser is racked up a layer of oil spreads out evenly between the top of the condenser and undersurface of the slide When the condenser is properly focused there is a pinpoint of bright light in the centre of the specimen The 1/12 oil immersion lens with funnel stop inserted is racked down to touch the oil on the upper surface of the

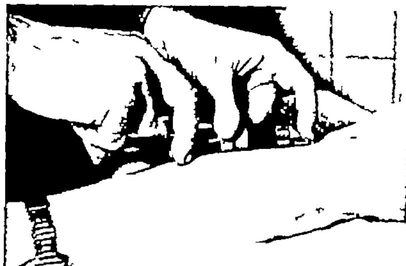


Fig 102.—Intravenous Injection
A two-handed technique avoids the possibility of the needle slipping out of the vein during injection

are sometimes used for the collection of specimens

In infants an easy way of collecting blood is to rub a heel with gauze until it is red, with the mother or an assistant grasping the leg above, and then to plunge a scalpel into it. The specimen tube is held under the wound and 2–3 c c. of blood are quickly collected Alternative sites in the infant are the superior longitudinal sinus entered through the anterior fontanelle or the external jugular vein

Intravenous Injection

The vein is entered in precisely the same way as already described When the needle is in the vein aspiration will cause blood to flow back into the fluid in the syringe. After this happens the tourniquet is released and the injection made Careful watch is kept to ensure that no leakage is occurring as evidenced by swelling around the needle or a complaint of pain or burning from the patient (Fig 102)

If no blood is aspirated the beginner will do well to withdraw the needle completely and start afresh. This should also be done if it is suspected that fluid is being injected outside the vein Another prick of a needle is much less trouble to a patient than an infiltration with an irritating drug

Catheterization of the vein by the needle is important in intravenous injection for it is possible to aspirate blood when the bevel is half way into a vein but when injection begins some of the fluid goes outside as well as into the vein The longer the bevel the likelier is this to happen

INTRAMUSCULAR INJECTION

Injections of bismuth and of some arsenicals are made intramuscularly and for this purpose the gluteal region will normally be chosen. In giving a series of injections the two sides will be used alternately To avoid injury or infiltration of the sciatic nerve, to miss the large blood vessels, and to strike the deepest muscular part of the buttock, the injection should be made into the upper and outer quadrant The injection can be made with the patient lying prone or standing

If the prone position is used the patient lies on a couch with toes turned in and completely relaxed. If standing the weight is borne on the leg opposite to the side to be injected. The gluteal muscles on the side to be used are relaxed by making the patient bend this knee slightly and raise the heel.

The area is prepared with iodine or methylated spirit, and the needle, held by the butt or with syringe attached is plunged quickly through the skin which is stretched taut with the free hand and into the muscle for about one and a half to two inches (Fig 103) If the syringe has been used, it is detached, and if no blood exudes from the needle the syringe is replaced on the needle and the plunger pulled back to make sure that no blood vessel has been entered. If no blood is aspirated, the injection is made, the needle quickly withdrawn and the buttock firmly and deeply massaged The patient should continue the massage for two or three minutes afterwards If blood is aspirated, the needle is withdrawn entirely and inserted in another place.

The needle is never inserted right up to the butt because this is the point at which fracture is likeliest to occur The middle finger held down the shaft of the needle for a quarter of an inch below the butt acts as a buffer in making the injection and stops too deep penetration



Fig 103.—INTRAMUSCULAR INJECTION
Top muscles relaxed and skin held taut middle finger along needle to prevent its entry up to hub *Bottom*, needle in position

LUMBAR PUNCTURE

Properly performed lumbar puncture is no more difficult or dangerous than an intravenous injection and can be almost painless The best position for the test is with the patient sitting on a chair or couch with his feet on a stool or another chair so that the thighs are flexed up on the abdomen The arms are folded over the knees and the neck is flexed forward the forehead resting on the arms (Fig 104)

The test can also be done with the patient lying on his side on a rigid couch with a pillow under his middle to keep the spinal column straight. The arms clasp the knees which are flexed up on the abdomen, and the head is bowed forward In every case the aim is to produce backward bowing of the spinal column so that the spinous processes are sprung apart as far as possible. With the patient in position the iliac crests are found and the interspinous space nearest this level is chosen for the puncture. A pencil cross can be made with its centre at the middle of the chosen space to act as a guide.

The back is widely painted with tincture of iodine The operator now scrubs up completely but gloves need not be worn. Next, the skin is anaesthetized by raising a wheal with 2 per cent novocaine in the centre of the chosen space and the needle pushed forward for about an inch as a seeker and to anaesthetize the track of the lumbar puncture needle

While waiting for a minute for the novocaine to act the patient is told that he must not move during the operation and it is explained that the only thing he is likely to feel is possibly a twinge of pain down one leg

The operator sits behind the patient with his eyes on a level with the chosen space and holds the lumbar puncture needle, with its stilette inserted firmly near the butt in his right hand The needle has been sterilized by boiling after having been newly sharpened The point of the needle is bored through the anaesthetized skin as nearly as possible in the middle line and midway between the two spinous processes bounding the space Once through the skin the needle is pushed straight ahead in the horizontal plane and in most cases will meet no bony resistance. At a depth of two to three inches there is felt a slight resistance as the needle punctures the theca. The stilette is now removed and fluid should begin



Fig 94.—LUMBAR PUNCTURE IN THE SITTING POSITION

Line is at level of iliac crests left forefinger is on lumbar spinous process and dots show others

to drop from the bore of the needle. If no fluid appears, rotate the needle or advance a fraction of an inch and it will start to run if the end has merely been occluded by the membranes As the needle enters the canal a twinge of pain in the leg indicates that a branch of the cauda equina has been touched but no damage need be feared

The needle should not be pushed across the canal into the far wall or an intervertebral disc may be punctured If during insertion bone is encountered by the needle-point withdraw to skin level and depress or lift the point and try again Use no force, or pain will be caused and the needle may be broken. If entirely unsuccessful do not push the needle about for too long and traumatize the tissues, but start again in the next space up or down If still unsuccessful, proceed no further but send the patient to a specialist

When the fluid starts to run let the first few drops go to waste as they may be contaminated with blood then collect about 5 c c. in one test tube and 2 3 c.c. in another letting the fluid drop out slowly controlling flow with the tip of the stilette at the needle s orifice The specimen collected draw the needle firmly out, taking care not to bend it and risk its breaking A pad of gauze can be stretched over the puncture wound but it is not essential

The patient lies down on his face in bed and rests so for a few hours. He then may roll over but must stay recumbent for at least twelve and better twenty-four hours. Very nervous patients can be given an injection of ¼ grain of morphia half an hour before operation and it is a good plan to give all cases 1½ grains of Seconal one hour before and repeat the dose at night. No reading is allowed and the patient should use bottle and bed-pan on the day of operation

For this reason it is best to have the patient in hospital or

nursing home or perform the operation in his own home. Post puncture headache can be almost entirely eliminated if the patient lies for forty-eight hours recumbent, and is not common after twenty four hours rest. Lumbar puncture on ambulant cases is not advised, but if it has to be done the patient should be made to lie down in the consulting room for a few hours and then go straight home to bed. Headache can be controlled with aspirin or Veganin if it occurs. It usually lasts for forty-eight hours at most, but may sometimes persist as long as ten days The smaller the needle used and the defter the operator the less likely is post puncture headache.

The type of needle used matters little provided it is fine and of good quality steel or nickel. It should be sharpened before each operation, the bevel being made fairly short, and tested for flexibility to avoid fractures in use. For general purposes the White-Jeanselme or Rochester Row needles are satisfactory

DORSAL SLIT AND CIRCUMCISION

The two operations will be considered together because dorsal slit is a preliminary to the method of circumcision here described

If there is no gross oedema and sepsis, local anaesthesia with 2 per cent novocaine and adrenalin is best. There is practically no bleeding and the patient is little disturbed In the presence of sepsis a general anaesthetic is used, the method being at the discretion of the anaesthetist.

It is best for the patient to keep to bed for twenty-four to forty-eight hours after operation but with local anaesthesia many a patient has performed a day's work after the operation and been none the worse. The operation can even be performed in the consulting room and the patient sent home to rest immediately afterwards.

The hair should be clipped or shaved round the base of the penis and subpreputial washing is given if necessary before the operation. 1½ grains Seconal half an hour before the operation is a good sedative. An assistant, not necessarily skilled is required

The Operation (Fig 105)

The patient lies recumbent with the penis exposed through

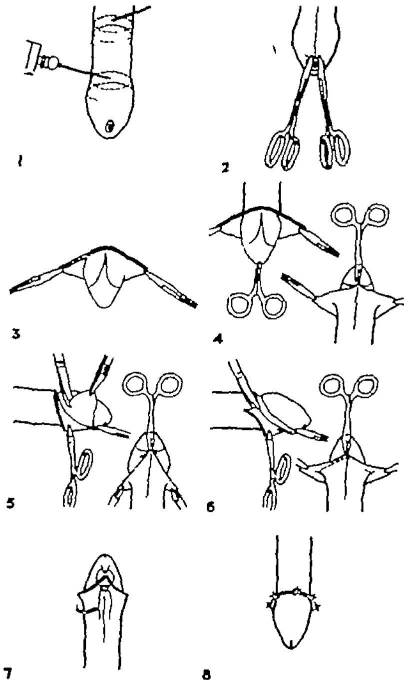


Fig 09.—Circumcision

1 Levels for injection of novocain line of dorsal slit in prepuce; 3, dorsal slit complete; *forceps hold skin*; *inner layer of prepuce shown lying on glans* 4, guide forceps on median raphe: level to which prepuce is to be removed; 5, *removing inner mucous layer of prepuce*; 6, *removing outer skin layer of prepuce* along dotted lines; 7 frenal stitch: goes through skin, across stump of frenum and out through skin again; 8, remainder of stitches in position

sterile coverings A ring of novocaine is made in the deep subcutaneous tissues round the base of the shaft. This can be done with only two insertions of the needle and can be practically painless. After two minutes sensation is dulled and another ring of anaesthesia is made just behind the level of the coronal sulcus If possible the prepuce is retracted before doing this Special attention is paid to ensure that the frenal region is well infiltrated. In another two or three minutes cutting can begin. The patient may feel touch on the glans and this should be explained to him.

Stage 1 Dorsal Slit

Clamp two Spencer-Wells forceps on the middle of the dorsum of the preputial orifice. These are held up and apart by surgeon and assistant and a bold cut is made with blunt ended scissors dividing the prepuce down to the coronal sulcus Take care not to put the inner scissors blade down the urethra by mistake

In phimotic cases the glans is now exposed and any con cealed sores are revealed If this is all that is required or if complete circumcision is considered impossible because of the condition found the wound is now dressed with gauze soaked in saturated magnesium sulphate or saline solution after any necessary specimens have been taken for pathological examina tion. It is rarely necessary to tie off bleeding points on the cut surfaces For exposure only some surgeons make two lateral slits instead of one dorsally but little is gained in exposure and the final cosmetic result is often worse than with a dorsal slit. Healing after a dorsal slit sometimes leaves a certain amount of redundant tissue which may have to be removed at a subsequent operation

Stage 2 Removal of Prepuce

Clamp a Spencer-Wells forceps on the *median ventral* raphe at the level to which the skin is to be removed. This should be at a point opposite the frenum when the skin is held up Starting from the end of the dorsal slit, cut with scissors round the inner layer of the prepuce about an eighth of an inch from the sulcus on either side right round to the frenum The frenum is cut across leaving a good tag for future stitching The skin is held aside by forceps, and the glans by means of a

gauze swab held by the assistant to give a clear field.

Next cut the skin with *scissors on either side, starting from* the end of the dorsal slit and aiming at the point of the forceps on the median raphe. The whole prepuce is now completely removed. Any bleeding points, and they are rare, can be *ligatured with* fine catgut.

Stage 3 Stitching

The ventral skin edge will taper to a point on the median raphe. With fine catgut on a small cutting needle, stitch through the skin across the frenum and out through the skin again This makes a good tether and controls bleeding from *the frenum. Next suture the two edges at the opposite pole* on the dorsal surface at a point corresponding to the original end of the dorsal slit Two or three evenly distributed sutures on either side will make all secure

Stage 4 Dressing

Friar s balsam or sterile vaseline on ribbon gauze can be used to dress the cut surface. This is covered with a moderately tight bandage and the penis is supported up over the abdomen with a T bandage and a pad of cotton wool. The dressing need not be changed for twenty four hours and thereafter is changed daily If sepsis occurs, eusol can be used as a dressing The catgut sutures start to fall from the fifth day onwards, but can be removed after the seventh day If there is no sepsis a dry gauze dressing can be used after the first few days and *soaked off in warm saline solution when being changed* Most clean cases will be quite healed in ten to twelve days The patient can go about his duties normally in most cases.

The only likely complication is haemorrhage which infre*quently occurs in the first twelve hours after operation* This is seldom enough to require the use of a ligature and can usually be controlled with an adrenalin dressing and tight bandage. The cosmetic result of this method of circumcision is very much better than that obtained with the ritual circumcision for exactly the right amount of skin to be removed is judged A little oedema on the site of the frenal stitch sometimes remains for a week or two after healing but always disappears completely

FEVER THERAPY IN VENEREAL DISEASE

The use of induced high temperature has an important place in the treatment of the venereal diseases. In syphilis the chief indications for fever therapy are general paralysis of the insane, taboparesis and primary optic atrophy Combined high fever and arsenotherapy in early syphilis is still in the experimental stage, but preliminary reports indicate that in special circumstances it may have an application Fever therapy is useful in certain cases of sulphonamide resistant, and of complicated, gonorrhoea.

High temperature produces its therapeutic effect in two ways first, there is a lethal effect on the infecting agent and secondly tissue permeability to drugs is increased Maintained temperatures of 106 F and above are alone directly lethal but with lower temperatures the best results are only obtained by combining fever and chemotherapy

Many means of inducing fever have been tried and found successful, but only those in common use will now be considered Since malaria was first used in the treatment of general paralysis of the insane by Wagner von Jauregg the following among other methods have been used — relapsing fever protein shock, hot baths, long and short wave diathermy and fever cabinets

Hyperthermy (the term here defines the production and maintenance of temperatures of 106° F and above by means of fever cabinets) and malarial therapy are confined to hospital practice, but the general practitioner has at his disposal for the treatment of resistant and complicated gonorrhoea an excellent and safe method in intravenous T.A.B vaccine

Only patients in really good physical condition should be selected for fever treatment, and pulmonary tuberculosis and cardiovascular disease are absolute contra indications to its use. Fever therapy in selected cases of gonorrhoea and syphilis can sometimes accomplish in weeks what chemotherapy alone would take months, or even years, to do

T.A.B Fever

This method of inducing fever is used almost entirely in gonorrhoea, but it has been tried in neurosyphilis and is still

2 *Shock Cradle* A fever of up to 104 F can easily be induced by means of a simple cradle containing twelve electric light bulbs and placed over the patient in bed The patient lies on a covered rubber sheet and is wrapped in blankets and the cradle is covered over with more blankets, sealing in the patient up to his neck.

About two hours use of the apparatus is enough and the temperature is maintained by keeping the patient well wrapped up and with hot water bottles Care should be taken to avoid burning Results with this inexpensive apparatus in cases of gonorrhoeal rheumatism have been gratifying The same effect can be obtained by the use of Thermega electric blankets over and under the patient. Several layers of ordinary blanket and a rubber sheet should intervene between the patient and the heating elements

A temperature of 106° F can be produced by either of these methods, but control and regulation are very difficult Hyperthermy should only be administered by experts and with the proper apparatus.

3. *Fever Cabinets* A variety of cabinets for the production of high fever has been used but the most popular is the Kettering Hypertherm. This is a box into which the patient can be slid on a stretcher leaving his head exposed. The box is airtight and the gap around the patient's neck is sealed Humidified air heated by means of a small electric radiator is circulated through the box and over the patient Sliding panels give access for the taking of blood pressure or for giving intravenous fluids and the patient can be removed on the stretcher in a few seconds if necessary

In any hyperthermy of this type the patient must be given constant supervision a high fluid intake by mouth, or intravenously if necessary must be maintained and the rectal temperature charted at very frequent intervals to avoid accidents. The patient's temperature is maintained at between 106 and 107 F for periods of from 4 to 12 hours. Hyperthermy is used in the treatment of both syphilis and gonorrhoea, but mainly in the latter

The fever cabinet was formerly used quite frequently for the treatment of sulphonamide-resistant gonorrhoea but it has now been almost completely displaced by penicillin. It is still the most effective method for treating gonorrhoeal arthritis

and the earlier it is used the better are the results. One or several treatment sessions may be necessary and it is usual to employ penicillin or a sulphonamide concurrently

Hyperthermy can also be used in the treatment of neurosyphilis instead of malaria but it has not displaced this latter method and both have their special applications. Both arsenic and penicillin have been administered during the course of fever sessions to enhance the effects and the results have warranted further experiments.

In early syphilis good results were obtained with a one day treatment in which arsenoxide was administered during a session of fever

High fever however produced, is a dangerous proceeding and must only be used by those who have had special training Its dangers and the sad lack of special equipment still impose limitations on its more frequent use.

PROPHYLAXIS OF VENEREAL DISEASES

Apart from complete abstinence from sexual intercourse the only method of prophylaxis which is likely to be effective in the majority of cases is the condom The condom has an added advantage that both parties are protected To be successful it must be used throughout the intercourse Even this is not 100 per cent efficient for contamination may take place by breakage or leakage of the condom from contamination by contact with infectious material on its removal or from para or extra-genital sores

Combination of the condom with chemical prophylaxis, to be described comes as near to complete efficiency as is possible.

Chemical Prophylaxis

Any post-coital prophylactic measures must be taken as soon as possible after the exposure. The possibility of success against a syphilitic infection is slight after one hour and nil after eight hours With gonorrhoea the limit of safety is about twelve hours

If a man reports within a few hours of exposure, the following procedure should be adopted.

(1) The patient urinates and then washes the genitals,

thighs and lower abdomen thoroughly with soap and water for about five minutes

(2) An anterior irrigation with 1 10 000 solution of potassium permanganate is given by the physician An alternative is the instillation of a drachm of 2 per cent Protargol solution into the urethra to be retained there for five minutes before it is allowed to escape

(3) The patient rubs 33 per cent calomel ointment into the penis and scrotum for five minutes The genitalia are wrapped in a paper towel to protect the clothes and the patient is told he should not urinate for four or five hours

If a man reports between twelve and twenty-four hours after intercourse, it is the author's practice to give, apart from the above preliminaries, an irrigation on the two following days This should be successful against gonorrhoea but is too late to be effective for syphilis.

Such a patient should be advised to have a blood test at least once a month for three months, and to report at once if any signs of disease appear

If nothing else is available, thorough washing with soap and water is fairly effective against soft chancre and syphilis and urinating in bursts may have some mechanical effect against urethral contamination

Chemical prophylactics of various mercurial and silver compounds can be bought for immediate use. How effective they are is quite unknown, but they should certainly be used with routine washing if available

Women almost never request prophylactic treatment, but if the occasion arises, J E Moore (*Modern Treatment of Syphilis*) advises this treatment

(1) Patient urinates She is placed in the lithotomy position and genitals and surrounding areas are washed with soap and water Douches of two quarts of sterile water followed by two quarts of 1 2000 mercury perchloride solution are given

The entire vaginal wall (using speculum) and vulva are swabbed with fresh 2 per cent Protargol solution and the same solution is injected into the urethra and held there for five minutes.

(2) Douche with sterile water and sponge dry with gauze Apply calomel ointment to cervix, vagina vulva and adjacent

parts, taking ten minutes over the operation. Cover the parts with a paper towel and instruct the patient not to wash for several hours

Any benefits which might accrue from prophylaxis will never be realized in civilian practice, because most venereal infections are contracted under influence of alcohol and enforced preventive measures are impossible.

Patients should be instructed in the theory of prophylaxis when they are being discharged after treatment for venereal disease.

Chemotherapeutic Prophylaxis

Arsphenamine and neo-arsphenamine have been advocated for use as prophylactic agents in suspected cases of syphilitic infection There is no experimental or practical evidence to show that such a method is reliable. Further such treatment might merely suppress the infection and there is always the risk of grave toxic reactions

Oral acetarsol has also been put forward as a prophylactic in syphilis, but the same counter-arguments hold good

Sulphathiazole has been tested as a prophylactic against gonorrhoea and chancroid

In controlled series significant reductions in the incidence of both diseases have been noted by American observers One method consists in giving, on the day after exposure, 3 gm of sulphathiazole at 8 A.M., 2 gm. at noon, and 1 gm. at 6 P.M. In another series, service men were given 2 gm. sulphathiazole before leaving camp 2 gm. on their return and 2 gm. the next morning

Prophylaxis in Doctors and Nurses

Doctors who work with bare hands are liable to extra genital infections Ear nose and throat surgeons, obstetricians gynaecologists and dentists are most commonly infected

When the ordinary precaution is taken of washing the hands in soap and water immediately after operating the risk is very slight.

Operations except of urgency on patients with early syphilis should be delayed until the patient has had at least three months treatment. Patients with infections more than four years old are usually not dangerous

If a surgeon pricks himself with a needle while operating on a potentially infectious case, the puncture should be incised to its approximate depth, allowed to bleed while washing under a tap and packed with 33 per cent calomel ointment for twenty-four hours.

If a patient coughs on the face of a doctor soap and water vigorously used at once should be sufficient. The conjunctival sac if contaminated should be washed out with saline solution and 5 per cent Argyrol instilled

APPENDIX I

SOCIOLOGY OF VENEREAL DISEASES

Until quite recently the education of the lay public on the subject of the venereal diseases was almost entirely neglected. In spite of this the incidence of venereal diseases was decreasing in Britain until 1939. The war has, however produced an alarming increase in these diseases and the incidence of fresh cases of syphilis is now about 70 per cent above the pre-war level. From this has come some good in that it has become necessary for the authorities to initiate an educational drive through the press and radio to inform the public on the recognition, facilities for treatment, and prognosis of the common venereal diseases.

Further legislative measures have been provided for the compulsory treatment of a certain type of sufferer from venereal disease. Regulation 33B makes it possible to compel examination and if necessary treatment by a special practitioner in the case of an individual who has been named as the source of infection by two or more persons. Notification is made to the Medical Officer of Health of the county or county borough in which the suspect person is living, but no action can be taken unless at least two accusations have been made. Such notifications can only be made by a special practitioner (one recognized by the Public Health Authorities as specially qualified in the diagnosis and treatment of venereal diseases) who is satisfied of the diagnosis in the case of the complainant. Malicious accusations are thus made most unlikely The individuals at whom this regulation is aimed are those who to quote the Ministry of Health, are impervious to methods of education and persuasion and who refuse to attend for treatment although known to be infected and to be spreading infection" Should an individual brought to treatment under Regulation 33B default before the treatment is completed he or she may be compelled to return. A doctor who is not a special practitioner and who wishes to make a notification under Regulation 33B can only do so in co-operation with a special practitioner who will naturally require pathological confirmation of the diagnosis in the case of the complainant. The County Medical Officer of Health will advise practitioners on any points arising out of the administration of this regulation.

In Britain the treatment of venereal diseases is voluntary except for those individuals who come within the scope of Regulation 33B.

The Public Health (Venereal Diseases) Regulations of 1916 provide for treatment centres where anyone may apply for free diagnosis and treatment, for the supply of approved drugs by medical practitioners, and for education of the public on the venereal diseases. By the Venereal Diseases Act of 1917 no person other than a *registered medical practitioner may treat venereal diseases* and the advertisement of drugs purporting to prevent or cure venereal diseases is forbidden. If one of the partners to a marriage was suffering from venereal disease in a communicable form at the time of marriage a decree of nullity may by the Matrimonial Causes Act of *1937 be granted by the court.*

It is the opinion of many people who are concerned with the problem of venereal diseases control that these provisions are not enough and that further measures for compulsory treatment will be required before any impression can be made.

In Sweden an admirable control system is in operation. Treatment is compulsory but facilities are free both for in-patients and for out-patients. Notification does not disclose the patient's name. *The source of infection and any contacts of the infected individual* can be compelled to attend for examination and for treatment if necessary. Legal powers are available to deal with patients who default from treatment while still infectious. In practice 97·5 per cent of cases attend until they are certified free of venereal disease in a communicable form, and *legal intervention is very rarely needed.*

In a community which had been given adequate education about the venereal diseases, a system such as that of Sweden could work admirably. Compulsion would seldom be necessary because the layman would have been instructed in his obligations to himself and to his fellow citizens. Until this Utopian state is attained there is still a great deal that the conscientious practitioner can do to help in the broad field of venereal disease control. He can try to ensure completion of *treatment to examine and treat the* contacts of his patients, and to reduce the incidence of congenital syphilis by routine blood testing in pregnancy. The taking of a sample of blood is easy and should never be neglected in any condition where the slightest possibility of syphilis exists.

Contact Tracing

It is the duty of anyone who treats venereal diseases to try to ensure *that the contacts of his* patients are brought under observation and if necessary treatment. All the contacts of an infected person should be investigated, not merely the one who is suspected of being the source of infection.

Only too often a person incubating a venereal disease un-

wittingly exposes others to infection, a marriage partner being the commonest victim. In such a case the man should be advised to tell his wife — or vice versa — and the physician should arrange to see them both together and explain the position. In this way by the exercise of tact, major family disturbance can often be avoided.

If a contact lives in another vicinity the patient should write and advise him or her to seek a specialist's advice at once, either privately or at the nearest venereal diseases clinic. A detailed list of all such clinics in Great Britain and Ireland can be obtained from the Ministry of Health, Whitehall, London, S W 1

A contact of a patient with a venereal disease must not be casually dismissed as uninfected on the results of one negative examination. Observation should be continued at intervals of one or two weeks over a period of at least three months, and in the case of syphilis this is often a bare minimum, to cover the longest possible incubation period and allow for the appearance of a positive Wassermann reaction If the reason for the long period of observation is explained at the outset, little difficulty is experienced in ensuring attendance. In the case of a patient with congenital syphilis, the parents and siblings should be examined.

At this point attention is drawn to the need for care in the giving of medical certificates on the subject of venereal disease. It is best to avoid certification altogether and if any opinion is given it must be guarded and refer only to the patient's condition at the time of examination

In a properly organised and nation-wide scheme for contact tracing lies probably the best means of attack on the whole problem of venereal diseases. Contact tracing, properly done can assume enormous proportions and embrace an ever increasing circle as the contacts of the original contacts of any given patient are brought in. When specially trained nurses or visitors are employed to trace contacts, explain the reasons why they should have medical examination and bring them to a clinic, the percentage of successful interviews is extremely high. This method of approach is still only possible on a very small scale in Britain, but it has achieved striking success where it has been used in the United States.

Defaulters

On the attitude which the physician adopts towards his patients depends largely the number of defaulters from treatment. If the doctor gives the impression that a patient with venereal disease is a leper and fortunate that anyone will treat him at all he cannot expect to establish the relationship of mutual trust which is so important in such cases.

The patient who stops treatment before cure can be a danger to the community and may jeopardize his own immediate or future health. A frank explanation of the probable course of the disease and of the estimated length of treatment should always be given as soon as a diagnosis is made. *At every visit it should be reiterated* that regularity of treatment is, particularly in syphilis just as important as the total amount.

If the doctor can, by a firm but sympathetic attitude, gain the confidence of his patient, the latter if he defaults, will not resent inquiries as to the reason for his lapse. A high defaulter rate merits an investigation to discover whether the fault lies in demeanour or in faulty technique. The best bedside manner cannot impress a patient whose arm has been mutilated by an extravenous injection of neo-arsphenamine

Marriage

The importance of examining the partner in the case of married individuals with venereal disease cannot be over-stressed The patient is often loath to consent to this, but if the history suggests that the infection may have been passed the strongest pressure should be brought to bear Sexual intercourse is forbidden, when both partners are affected until both have been pronounced cured If this order is not obeyed, mutual re-infection, notably with gonorrhoea can go on interminably

Marriage should be forbidden until a patient has had a final test of cure in gonorrhoea and until a year has elapsed without incident after full treatment for syphilis

A woman who has syphilis must be told to avoid pregnancy until she is cured and has completed two years of uneventful observation. Even then she should have treatment during every subsequent pregnancy as a precaution.

A blood test should be a *routine* for every pregnant woman no matter what her social status, on her first visit for ante-natal advice If this were done the amount of congenital syphilis would be reduced to negligible proportions.

In some countries it is necessary before a marriage can be solemnized, for both parties to produce certificates stating that they have been examined and found to show no evidence of venereal disease. A negative blood test for syphilis from a reliable laboratory must also be produced Until this admirable system is introduced in Britain, the practitioner should always have at least a blood test for syphilis done *on any patient* who consults him for any reason before marriage.

APPENDIX II

LIST OF SPECIAL EQUIPMENT

Essential

10-c.c. syringes.

2-c.c. syringes.

Needles — intravenous, intramuscular hypodermic and lumbar puncture.

Arkansas stone for sharpening needles.

Platinum loop.

Glass slides and cover-slips.

Tubes for blood specimens.

Capillary tubes for serum specimens.

Stains — methyl violet, Lugol's iodine neutral red.

Urine glasses.

Irrigation outfit — adjustable stand, container tubing and Janet nozzles.

Vaginal douche nozzles.

Vaginal specula — assorted sizes Fergusson's or Cusco's or both.

Playfair's probes.

Vaginal sponge-holders or forceps.

Urethral sounds — set of Lister's or Clutton's sounds or both.

Gum elastic bougies — one set.

Catheters — gum elastic and rubber

Useful Accessories

Combined operating table and lithotomy chair

Straight bougies — one set, Bayly's or Wyndham Powell's.

Filiform and whip bougies.

Urethroscope Harrison type

Electrocautery with assorted points.

Microscope with $\frac{1}{12}$ objective. Dark-ground condenser

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